“A PROSPECTIVE, RANDOMIZED STUDY COMPARING THE ANALGESIC EFFECTS OF INTRAVENOUS NALBUPHINE WITH INTRAVENOUS TRAMADOL ON POSTOPERATIVE PAIN AND POSTOPERATIVE ANALGESIC REQUIREMENT FOR PATIENTS UNDERGOING PERCUTANEOUS NEPHROLITHOTOMY”.

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE

MADRAS MEDICAL COLLEGE

CHENNAI- 600003

APRIL 2016

CERTIFICATE

This is to certify that the dissertation entitled, **"A PROSPECTIVE, RANDOMIZED STUDY COMPARING THE ANALGESIC EFFECTS OF INTRAVENOUS NALBUPHINE WITH INTRAVENOUS TRAMADOL ON POSTOPERATIVE PAIN AND POSTOPERATIVE ANALGESIC REQUIREMENT FOR PATIENTS UNDERGOING PERCUTANEOUS NEPHROLITHOTOMY"** submitted by **Dr. M.SURESH** in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamil Nadu Dr. M.G.R. Medical University, Chennai., is a bonafide record of the work done by him in the INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and Government Hospital, during the academic year 2013-2016.

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DECLARATION

I hereby, solemnly declare that this dissertation entitled **"A PROSPECTIVE, RANDOMIZED STUDY COMPARING THE ANALGESIC EFFECTS OF INTRAVENOUS NALBUPHINE WITH INTRAVENOUS TRAMADOL ON POSTOPERATIVE PAIN AND POSTOPERATIVE ANALGESIC REQUIREMENT FOR PATIENTS UNDERGOING PERCUTANEOUS NEPHROLITHOTOMY",** is a bonafide record of the work done by me in the Institute of Anaesthesiology and Critical Care, Madras Medical College and Government General Hospital, Chennai, during the period 2013 – 2016 under the guidance of **DR. B.KALA, M.D., D.A.,** Director, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai – 3 and submitted to **The Tamil Nadu DR. M.G.R. Medical University, Guindy, Chennai – 32**, in partial fulfilment for the requirements for the award of the degree of M.D. Anaesthesiology (Branch X), examinations to be held on April 2016.

I have not submitted this dissertation previously to any university for the award of degree or diploma.

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Date:

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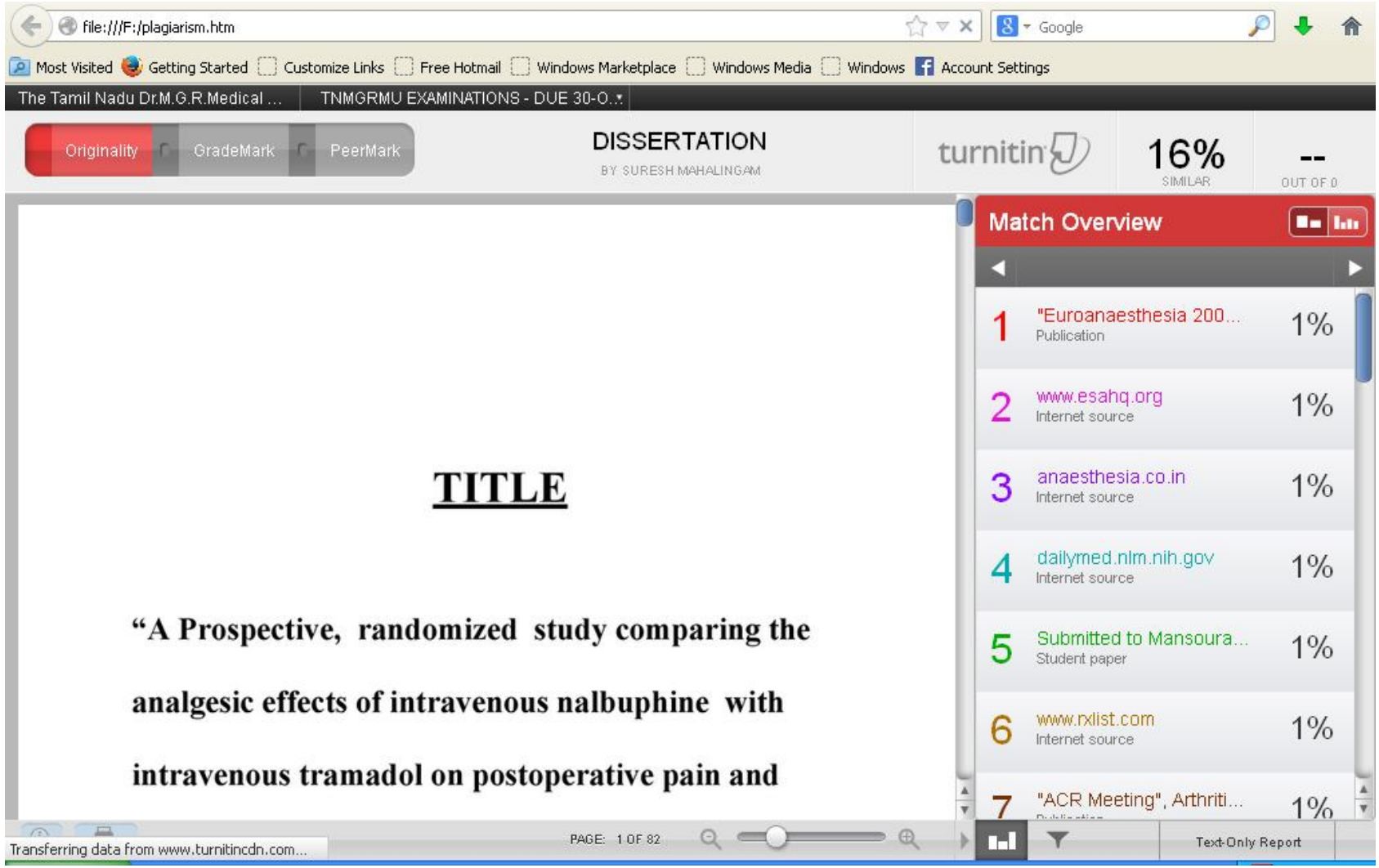
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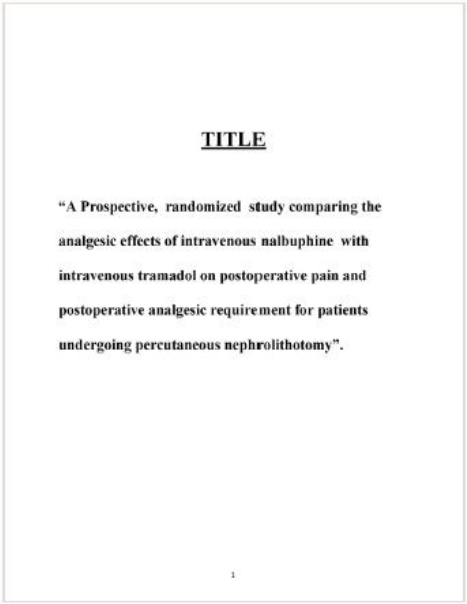


TITLE

"A Prospective, randomized study comparing the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy".

1

CONTENTS

AIM OF THE STUDY:

This study compares the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy(PCNL).

ABSTRACT:

Post-operative pain produces both acute and chronic effects. Attenuation of this pain results in attenuation of the stress response, which in turn decreases the complications and facilitates recovery during the immediate post-operative period.

The usage of nalbuphine and tramadol when administered intraoperatively, maintains better post-operative hemodynamics , causing excellent post-operative pain relief. There have been few studies using intravenous nalbuphine and intravenous tramadol for postoperative analgesia.

In this study, we randomly selected 60 patients and divided them into two groups. GROUP A received a bolus dose of Nalbuphine 0.2mg/kg, 30 mins before extubation and GROUP B received a bolus dose of Tramadol 1mg/kg, 30 mins before extubation. The primary outcomes measured were Post-operative visual analog score and Systolic blood pressure(SBP), diastolic blood pressure(DBP), mean arterial pressure(MAP), heart rate(HR), respiratory rate(RR) and oxygen saturation(Spo2). The secondary outcomes measured were Post-operative rescue analgesic initiation time and Side effects and any other complications.

RESULTS:

The mean visual analog score was less in nalbuphine group when compared to the tramadol group from 30 minutes to 8 hours time intervals, which was statistically significant. The duration of action of both the drugs was about 8 hours as the time to rescue analgesia was similar in both the groups.

In both the groups , the hemodynamic changes and respiratory parameters in the post operative period were comparable and statistically insignificant. The nalbuphine group showed an increased occurrence of drowsiness, while the tramadol group showed an increased occurrence of nausea and vomiting.

CONCLUSION:

From my study, I conclude that nalbuphine appears to be an effective and safe analgesic for postoperative pain relief than tramadol in equianalgesic doses, in patients undergoing percutaneous nephrolithotomy, providing good sedation with minimum circulatory effects.

INTRODUCTION

Nephrolithiasis[1] or stone in the kidney is a common problem, whose incidence is increasing. The prevalence of nephrolithiasis is 10% in men and 5% in women. There are many types of kidney stones. Most commonly the stones contain calcium. Other types include oxalate, citrate, cysteine stones. Non-contrast ct scan is most commonly used for its diagnosis. Patients with renal stones usually present with intermittent or continuous severe colicky pain in the flank and upper abdomen.

Conservative non-surgical therapy for small stones consists of analgesics (eg. NSAIDS and opiates) and aggressive fluid administration to promote urine flow and stone passage. Medical expulsive therapy, which promotes ureter relaxation and spontaneous passage involves treatment with calcium channel blockers, alpha-blockers and corticosteroids. If the stones are resistant to these methods, then surgical intervention is needed.

Percutaneous nephrolithotomy is generally done for the management of large intranephric stones, mainly those resistant to shock wave lithotripsy, staghorn calculi and some proximal ureteral stones.Initially a ureteral stent is kept in lithotomy and then patient is repositioned to the prone position for the percutaneous puncture. General anaesthesia with endotracheal intubation is commonly used for this procedure. It allows for a secure airway for positioning into the prone position.

Nalbuphine and Tramadol when administered intravenously intraoperatively, tend to maintain better post-operative hemodynamics causing excellent post-operative pain relief. Hence the ill effects of post-operative pain are prevented by the two drugs.

AIM OF THE STUDY

To compare the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy" , based on

PRIMARY OUTCOME MEASURES :

- Post-operative VAS score
- Systolic blood pressure ,diastolic blood pressure, mean arterial pressure, heart rate, respiratory rate and oxygen satuiration were measured at baseline and at intervals of 1,5,10,15,30min and 1,2,3,4,5,6,8,10,12 and 24hours.

SECONDARY OUTCOME MEASURES :

- Dosage of rescue analgesic requirement

PERCUTANEOUS NEPHROLITHOTOMY

Percutaneous removal of kidney stones – also known as percutaneous nephrolithotomy (PCNL) – had been found out around thirty years ago. Fernstrom and Johansson (1976)[2] first reported the creation of a track for this. This technique was then taken up by many other places , mainly by Wickham et al (1981) and Alken et al (1981). It has been evolved since then and refined with the invention of new endoscopes and various other accessories.

Percutaneous nephrolithotomy is a procedure used for stone removal from the kidney. Percutaneous means 'through the skin' and nephrolithotomy means 'taking the stones out of the kidney'. The surgery is done telescopically.

INDICATIONS :

- Stones which are bigger than 1.5 cms in the kidneys or the ureter.
- Stones which are bigger than 1cm occurring in lower pole.
- Staghorn-- shaped stones.
- Stones in calyceal diverticulum
- Stones refractory to other treatments
- Stones with UPJ obstruction or poor drainage like horseshoe kidney.
- Patient choice

CONTRAINDICATIONS :

- Absolute contraindications - any active infection, presence of coagulopathy, pregnancy, and an unsafe access
- Relative contraindications – presence of cardiac or pulmonary disease, and morbid obesity.

Anaesthesia and Positioning:

This surgery should ideally be done under general anaesthesia, since the patients have to lie for long duration of time in a relatively uncomfortable position, often extending up to three hours. However, it could be done under sedo-analgesia if it is done as a staged procedure.

Percutaneous puncture is the most difficult step. Correct puncture is facilitated by the proper positioning , which also protects the anaesthesised patient from any injury. The positions which are generally preferred for puncture are:

- Prone-oblique with the affected side tilted upside.
- completely prone, with the puncture performed from the posterolateral direction.

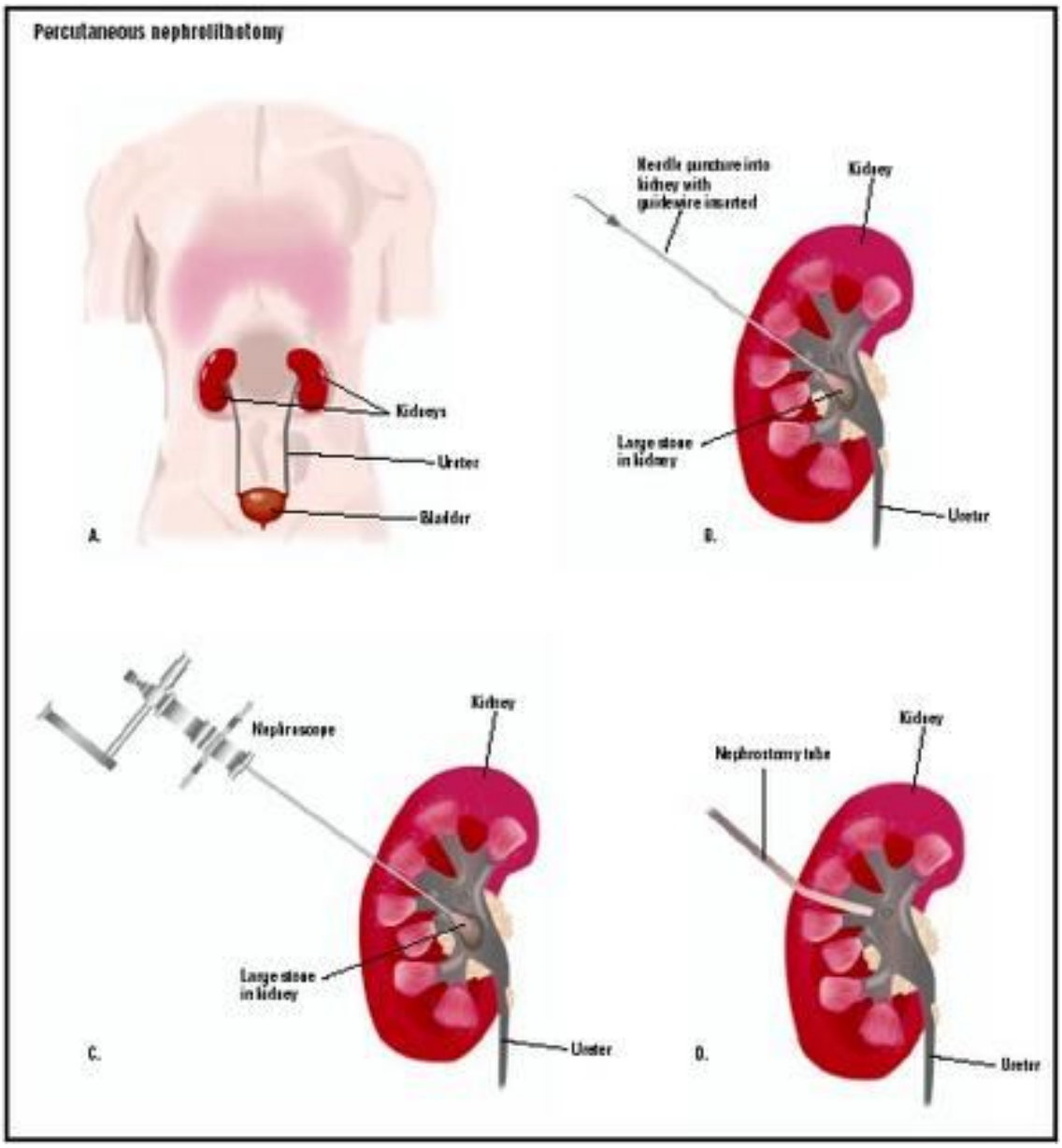
PROCEDURE :

The technique of percutaneous nephrolithotomy consists of three steps:

1. Puncture of pelvi-calyceal system which is done through the skin,
2. Development of the track,
3. Fragmentation and/or removal of the stone.

General anaesthesia is usually given for PCNL. The patient is initially in the supine position. Then the surgeon will perform a cystoscopy and will instill x-ray dye or carbon dioxide into the kidney to visualise the branches of the collecting system. This helps to identify the stone inside the kidney and for accessing the same using guidance.

The needle tract is then dilated to help in the placement of a plastic sheath and telescope to visualize the stone. The stone is then fragmented into small pieces using a mechanical, ultrasonic or laser lithotripsy device. It is then extracted out through the sheath. Sometimes, removal of all stones may require more than one tract to access the stones. A ureteral stent draining the kidney to the bladder may be left. Also a nephrostomy tube which drains the kidney will be present finally. A urinary catheter will be left in the bladder. An X-ray will be done on the following day to look for any residual stone that may be left in the kidney. An X-ray dye test is done through the drainage tube from the kidney, one or two days post operatively. The tube will be removed if the test is satisfactory. The expected hospital stay is for 4 to 5 days.



COMPLICATIONS :

This is relatively a safe procedure, but is associated with the following risks and complications.

- Bleeding: It is usually associated with some blood loss, which rarely requires blood transfusions. Autologous blood transfusion technique can be used3.

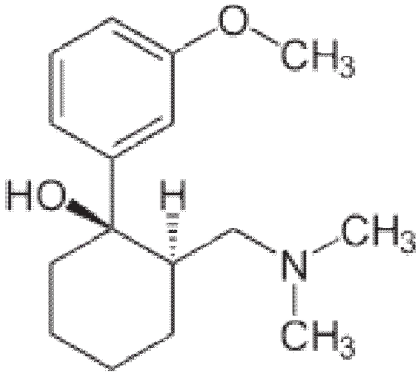
- Infection: Its occurrence is minimized by using broad-spectrum antibiotics after surgery.
- Tissue / Organ Injury: Eventhough it is uncommon, injury to bowel, liver, spleen, lung, , gallbladder, pancreas and vascular structures can occur. Loss of kidney function is a rare but serious risk. The formation of scar tissue in the kidney or ureter can occur.
- Conversion to open surgery: if there is difficulty encountered during this procedure. This would result in a bigger incision and a bigger recuperation period.
- Failure to Remove the Stone: Due to the size or location of the stones, in which case, additional treatment will be required.

PHARMACOLOGY OF TRAMADOL

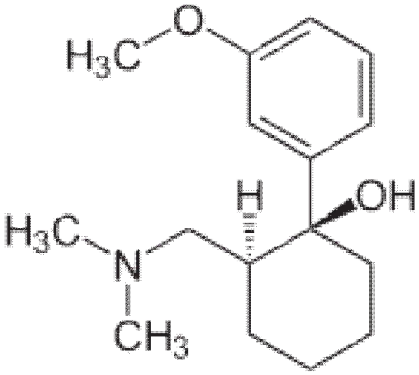
ACTIVE INGREDIENT: Tramadol hydrochloride

CHEMICAL NAME: 2-(dimethylaminomethyl)-1-(3-methoxyphenyl) cyclohexanol

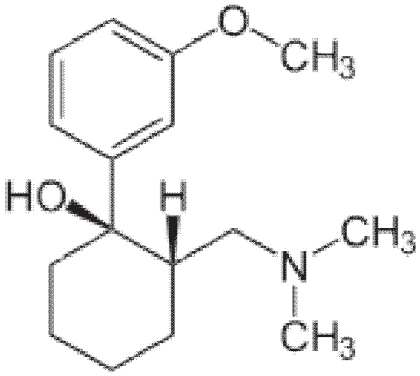
CHEMICAL STRUCTURE: Tramadol exists in four types of configurational forms:



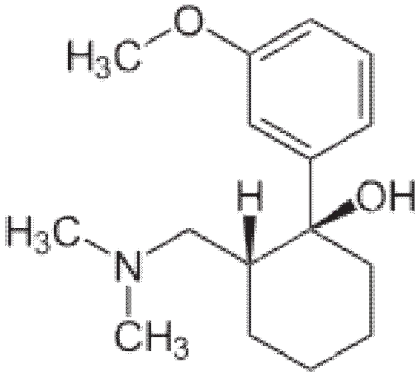
(1*R*,2*R*)-Tramadol



(1*S*,2*S*)-Tramadol



(1*R*,2*S*)-Tramadol



(1*S*,2*R*)-Tramadol

MECHANISM OF ACTION :

Tramadol is a centrally acting synthetic opioid analgesic 4,5. The mechanisms which appear to be applicable are:

- Tramadol is a pure agonist (non-selective) at mu, delta and kappa opioid receptors with a higher affinity for the mu receptors.
- Weak inhibition of reuptake of norepinephrine and serotonin and as a serotonin releasing agent.
- It also acts as an 5-HT2C receptor antagonist , NMDA receptor antagonist , (α7)5 nicotinic acetlycholine receptor antagonist, and as an antagonist at M1 and M3 muscarinic acetylcholine receptors. It is also a TRPV1 receptor agonist
- O-desmethyltramadol, tramadol's major active metabolite is a high-affinity ligand of δ- and κ-opioid receptors. Its activity at the δ-receptor could be involved in its ability to provoke seizures.

PHARMACOKINETICS:

1. Tramadol is well absorbed orally. It has a bioavailability of 75%.
2. Tramadol has a volume of distribution of 306 L after oral administration and 203 L after parenteral administration. It has a high tissue affinity.
3. It is 20% plasma protein bound.
4. Tramadol is extensively metabolized in the liver by a many pathways, including CYP2D6 and CYP3A4, and also by conjugation of parent and metabolites. The formation of M1 is dependent upon CYP2D6. N- and

O- demethylation and glucuronidation or sulfation in the liver are the major metabolic pathways.

5. Tramadol and its metabolites are excreted primarily in urine.
6. The plasma half-lives of tramadol and M1 are 6.3 and 7.4 hours respectively. Linear pharmacokinetics have been seen following multiple doses of tramadol of 50 and 100 mg to steady-state.
7. A serum concentration of 100 - 300 ng/ml is effective.

THERAPEUTIC USES :

It is indicated for treatment of moderate to severe pain in adults and adolescents aged > 12 years.

ROUTES OF ADMINISTRATION :

Tramadol is given either orally, intramuscularly or by intravenous injection(slow) or diluted in solution for administration by infusion or patient controlled analgesia. The usual dose is 50mg or 100mg given 4 to 6 hourly by either intramuscular or intravenous routes.

ADVERSE EFFECTS :

- Very common : nausea and vomiting
- Common: Feeling drowsy, headache, dry mouth, constipation, sweating
- Uncommon: palpitations, gastrointestinal irritation and utricaria.
- Rare: allergic reactions, blurred vision, convulsions, mood changes, tremors, urinary problems like difficulty in passing urine or urinary retention.

When the medicine is stopped, withdrawal symptoms can occur. These include hyperactivity, agitation, sleeping disturbances, nervousness, tremors, vertigo or gastrointestinal problems.

CONTRAINDICATIONS: Tramadol is contraindicated in

- Those having demonstrated hypersensitivity towards tramadol or any of the other ingredients.
- Those with seizure disorder which is not controlled by treatment.
- Those suffering from acute intoxication with centrally acting analgesics, alcohol, opioids, hypnotics or psychotropic drugs.
- Those who are on MAO inhibitors or within two weeks of their withdrawal.
- narcotic withdrawal treatment.

INTERACTIONS :

The following drugs interact with tramadol :

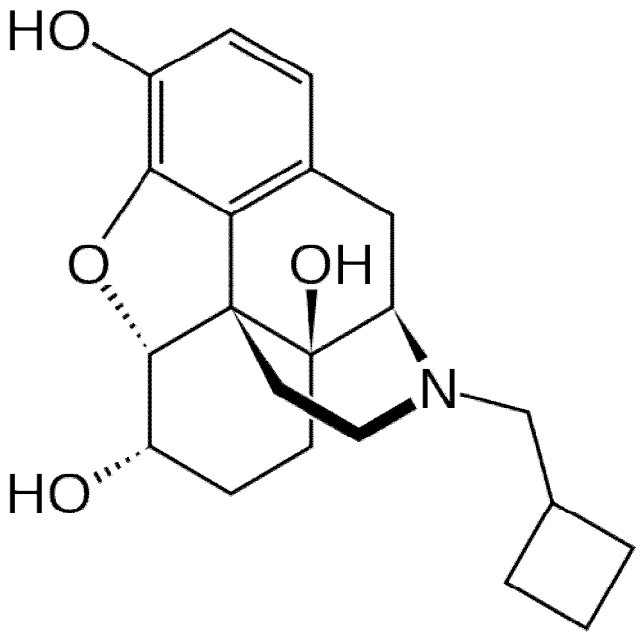
Antifungal medications (ketoconazole), Antibiotics (erythromycin and linezolid), Antidepressants like monoamine oxidase (MAO) inhibitors (phenelzine, isocarboxazid), serotonin norepinephrine reuptake inhibitors (SNRIs) (duloxetine and desvenlafaxine), tricyclic antidepressants (amitriptyline), and (SSRIs) (citalopram., fluoxetine), Migraine headache drugs (almotripta, frovatriptan), antiepileptics (carbamazepine), Blood thinners (warfarin), lithium, digoxin, Quinidine, Rifampin.

PHARMACOLOGY OF NALBUPHINE

ACTIVE INGREDIENT: Nalbuphine Hydrochloride

CHEMICAL NAME: (–)-17-(cyclobutylmethyl)- 4,5α-epoxymorphinan-3,6α,14-triol hydrochloride

CHEMICAL STRUCTURE: Nalbuphine is a synthetic opioid agonist-antagonist analgesic. It belongs to the phenanthrene series.

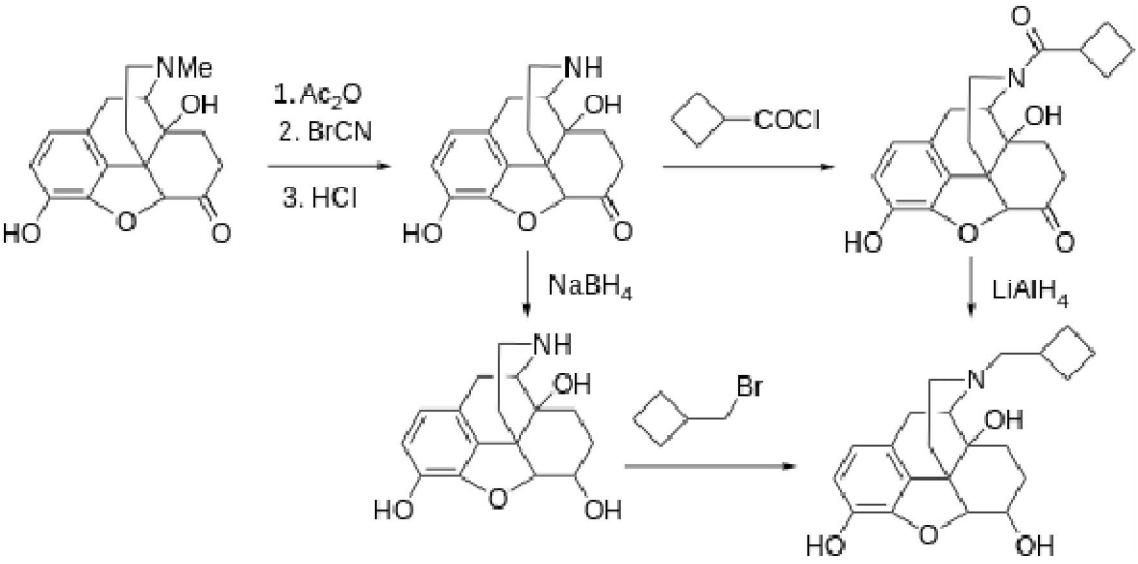


SYNTHESIS :

It is synthesized from oxymorphone, which reacts with cyanogen bromide (known as Von Braun reaction), giving rise to a N-cyano derivative. Subsequently, hydrolysis of this compound with hydrochloric acid gives rise to 14-hydroxydihydronormorphone.

The carbonyl group of 14-hydroxydihydronormorphone is reduced by Na hydroxide and then alkylated with cyclobutylmethylbromide, or acylated

with cyclobutanecarboxylic acid chloride and then reduction of both the carbonyl groups in the compound thus formed using lithium aluminium hydride leads to the formation of nalbuphine.



Each milliliter (mL) of Nalbuphine hydrochloride contains 10 mg or 20 mg of nalbuphine, 0.47 mg of sodium citrate dihydrate and 0.63 mg of citric acid, anhydrous which are added as buffers. It may also contain HCl and/or NaOH for pH adjustment. pH is 3.7 (3.0 to 4.5). It contains NaCl for adjustment of tonicity.

Multiple-dose vials usually contain methylparaben1.8 mg/mL and propylparaben added as preservatives. The single-dose products usually contain no bacteriostatic or antimicrobial agent.The portions which are not utilized have to be thrown away.

MECHANISM OF ACTION :

Nalbuphine binds to mu, kappa, and delta receptors[3]: but not to the sigma receptors. Nalbuphine hydrochloride is primarily a kappa agonist and partial mu antagonist analgesic. It is a potent analgesic and its potency is equivalent to that of morphine. It has an opioid antagonist activity of about 1/4 as potent as nalorphine and 10 times that of pentazocine.

PHARMACOKINETICS:

- Nalbuphine has an onset of action within 2 to 3 minutes after intravenous administration. It is less than 15 minutes following a subcutaneous, or intramuscular injection.
- The plasma half-life of Nalbuphine is 5 hours.The duration of analgesic activity has been found to be from 3 to 6 hours(≈5 hours).
- The bioavailability is about 81% (10mg) given intravenously.
- It is metabolized by the liver and ecreted in the urine.

THERAPEUTIC USES:

- Nalbuphine hydrochloride is used for the relief of moderate to severe pain.
- The drug has also been used as a treatment for morphine induced pruritus (itching).
- It can also be used as a supplement for balanced anesthesia.
- It is also used for preoperative and postoperative analgesia, and for obstetrical analgesia during labor and delivery.

- The opioid κ-receptor activation antagonizes the various opioid μ-receptor mediated actions in the brain.

ROUTES OF ADMINISTRATION :

It is administered subcutaneously, intramuscularly or intravenously. The recommended adult dose is 10 mg for a person weighing seventy kilograms. It may be repeated every 3 to 6 hours as necessary. In those who are not tolerant to the drug, the recommended single maximum dose is 20 mg. The maximum daily dose is 160 mg. The use of nalbuphine as a supplement to balanced anesthesia generally requires a larger dose than those recommended for analgesia.

Induction doses of nalbuphine - 0.3 mg/kg to 3 mg/kg iv administered over a 10 to 15 minute period along with maintenance doses of 0.25 to 0.5 mg/kg in single intravenous administarations.

ADVERSE EFFECTS:

- Nervous system - sedation (36%), dizziness/vertigo (5%), and headache (3%). Nervousness, restlessness, hallucinations, dysphoria, numbness, tingling, confusion.
- Cardiovascular system - hypertension, hypotension, bradycardia, and tachycardia.
- Respiratory - respiratory depression, dyspnea.
- Gastrointestinal - nausea/vomiting (6%) and dry mouth (4%). Cramps, bitter taste and dyspepsia have bben reported rarely.

- Dermatologic - itching, burning, and urticaria.
- Local side effects include pain, redness, swelling, burning sensations at the site of injection.
- Others – hypersensitivity reactions, urinary urgency, blurred vision, sweaty/clammy skin.

CONTRAINDICATIONS :

- Nalbuphine should not be given to patients who are found to be hypersensitive to nalbuphine or to any one of the other ingredients in it.
- Absolute: pseudomembranous colitis , diarrhea associated with toxins , respiratory depression , inflammatory bowel disease, acute asthma and sulfite sensitivity.
- It must be utilised with caution in hepatic or renal impairment, head trauma, increased intracranial pressure, morbid obesity and adrenal insufficiency. It can produce withdrawal in opioid dependent subjects.
- Also used with caution in pregnancy – can cause respiratory depression at birth, fetal bradycardia, cyanosis and apnea.

INTERACTIONS :

- Nalbuphine should not be used along with alvimopan. It increases the nalbuphine levels causing an increase in the side effects. It must be discontinued 7 days prior to usage of the drug.

- The combined use of nalbuphine with fentanyl, alfentanyl, buprenorphine and other opioid medications causes an increase in sedation and may cause withdrawal symptoms in narcotic addicts.
- Nalbuphine should not be used with MAO inhibitors like selegiline, phenelzine and isocarboxazid and linezolid (antibiotic) because they can increase nalbuphine toxicity. Nalbuphine administration must be isolated from the administration of MAO inhibitors and linezolid by atleast 14 days.

ANATOMY OF PAIN

Acute postoperative pain can induce change in the central nervous system, which is known as neuronal plasticity[6]. This results in sensitization of the nervous system, causing allodynia and hyperalgesia.

"The pain pathway is an afferent three-neuron dual ascending system, which receives descending modulation from the cortex, thalamus and brainstem. The nociceptors are free nerve endings, which are located in the skin, muscle, bone and connective tissue."

The first order neurons have their origin in the periphery as either A delta or C fibres.

A delta fibres - transmit first pain (sharp or stinging, well localized pain)

Polymodal C fibres – transmit second pain (more diffuse).

These 1st order neurons synapse with second order neurons in the dorsal horn. This synapse occurs primarily within laminas 1,2 and 5. This causes the release of neuropeptides and excitatory amino acids.

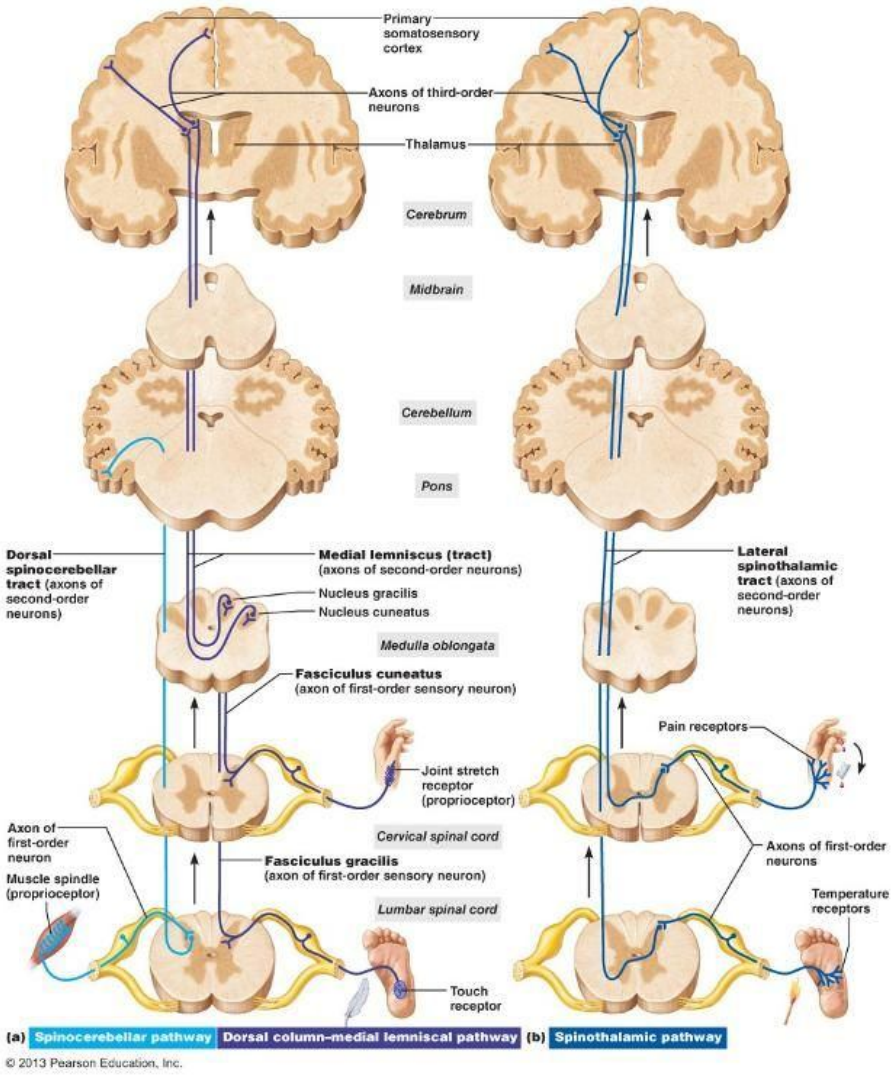
The second order neurons are of two types :

i. Nociceptive specific neurons – located mainly in lamina 1. They respond only to painful stimuli. They are mainly associated with sensory and discriminative aspects of pain.

ii. Wide dynamic range neurons – located in laminae4,5 and 6. They respond to both noxious as well as non-noxious stimuli. They are concerned with the affective and motivational aspects of pain.

'Axons of both these neurons go up in the spinal cord via the dorsal column- medial lemniscus and then the anterior lateral spinothalamic tract. Then they synapse on 3rd order neurons located in the opposite thalamus.

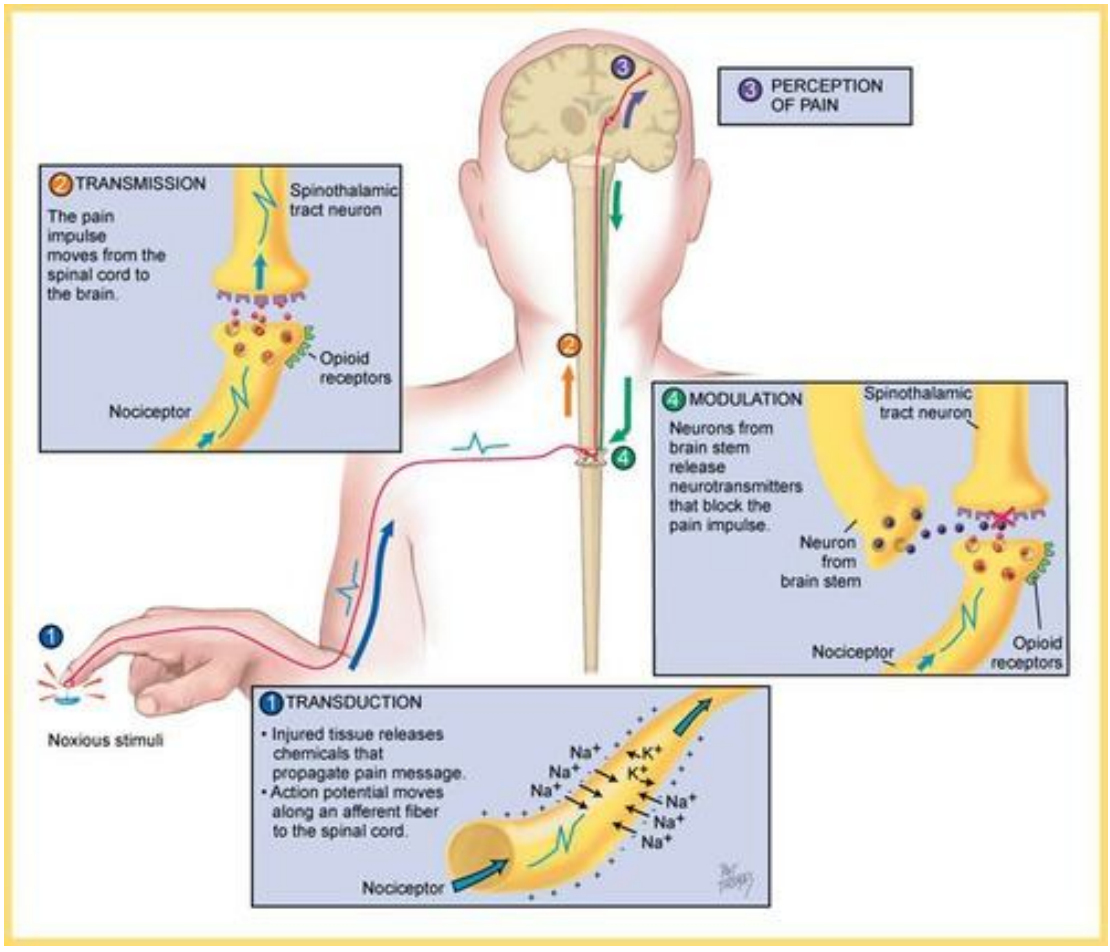
From the thalamus, there is projection to the somatosensory cortex, where pain is perceived.'



PAIN PROCESSING

The processing of pain is made up of 4 elements, namely

- Transduction
- Transmission
- Modulation and
- Perception.



1. **Transduction :** process by which noxious thermal, chemical/ mechanical stimuli are converted to an action potential.
2. **Transmission :** is the conduction of action potential through the 1^{st}, 2^{nd}, 3^{rd} order neurons, whose cell bodies lie in dorsal root ganglia, dorsal horn and thalamus respectively.
3. **Modulation :** refers to altering the afferent neural transmission along the pain pathway. It occurs mostly in the dorsal horn of spinal cord. It can resulr in either inhibition or augmentation of signals.

   Inhibitory – is by release of GABA and glycine in intrinsic spinal neurons.

   Spinal modulation causes augmentation, which is manifested as central sensitization.

   Eg . Repetitive C- fibre stimulation of wide dynamic range neurons in dorsal horn.
4. **Perception :** results from the integration of the painful input into somatosensory cortex and limbic cortex.

CHEMICAL MEDIATORS OF TRANSDUCTION & TRANSMISSION

The tissue damage following surgical procedures leads to the activation of nociceptive nerve endings and local inflammatory cells like macrophages, mast cells, lymphocytes etc. Antidromic release of substance P and glutamate occurs, which causes vasodilatation, plasma protein extravasation and stimulation of cells to release many allogenic substances.

Eg. Bradykinin, serotonin, histamine, prostaglandins, leukotrienes, cytokines, adenosine.

This will directly produce pain transduction via stimulation of nociceptors and also facilitate pain transmission by increasing the excitability of nociceptors.

Peripheral sensitization of C-fibres by these chemicals causes primary hyperalgesia – which is the exaggerated response to pain at injury site.

Dorsal horn of spinal cord has many transmitters and receptors associated with pain processing.

There are three classes of transmitter compounds :

- Glutamate and aspartate (excitatory amino acids)
- Substance P and neurokinin A (excitatory neuropeptides)
- GABA and glycine (inhibitory amino acids)

The different types of receptors are as follows :

- NMDA receptors
- AMPA receptors
- Kainate receptors and
- Metabotropic receptors.

AMPA and kainite receptors are Na channel dependent. They are required for fast synaptic afferent input. NMDA receptors are Ca channel dependent. They are activated following prolonged depolarization.

Substance P removes the magnesium block on the AMPA receptor channel, giving glutamate a free entry to NMDA receptors.

Repetitive C-fibre stimulation of wide dynamic range neurons can lead to central sensitization and wind-up. This causes secondary hyperalgesia, which is increased pain response evoked by stimuli outside area of injury.

EFFECTS OF POSTOPERATIVE PAIN

Post operative pain produces both acute and chronic effects.

Attenuation of this pain results in attenuation of the stress response[7], which in turn decreases the complications and facilitates recovery during the immediate post operative period.

ACUTE EFFECTS :

Transmission of the pain stimuli to the CNS causes the neuroendocrine stress response[8]. It is a combination of local inflammatory substances like cytokines, prostaglandins, leukotrienes etc and systemic mediators.

It results in increased sympathetic tone. This causes an increased release of catecholamines and other catabolic hormones (like cortisol, ACTH, ADH, glucagon, aldosterone, renin). The secretion of anabolic hormones is decreased.

This causes sodium and water retention and increased blood glucose, free fatty acids and ketone bodies level. There is also an increase in metabolism and oxygen consumption leading to a hypermetabolic, catabolic state.

The amount of stress response is directly proportional to the degree of surgical trauma.

It can also lead to the development of hypercoagulability, which leads to an elevated incidence of deep vein thrombosis, myocardial ischemia, and vascular graft failure.

It can also potentiate immunosuppression.

Hyperglycemia may lead onto depression of the immune function and poor wound healing.

Activation of the sympathetic nervous system also causes a delay in the return of gastrointestinal motility. This leads to paralytic ileus.

It can result in increased incidence of oliguria and urinary retention.

It can also result inanxiety, fear and frustration which leads to poor patient satisfaction.

Spinal reflex inhibition of phrenic nerve activity causes a reduction in the pulmonary function postoperatively. In the presence of poorly controlled pain, patients tend to take inadequate breaths and have an inadequate cough, leading to severe pulmonary complications like atelectasis, pulmonary infections etc.

CHRONIC EFFECTS :

Chronically occuring postsurgical pain is seen in about 10-65% patients[9]. Few of them have severe chronically occurring postsurgical pain.

It is mainly due to poorly controlled acute post operative pain.

This can lead on to long term behavioural and neurobiological changes.

PAIN ASSESSMENT METHODS

Assessment should commence pre-operatively as it can be valuable to estimate the patient's expectation of pain relief. When considering a postoperative regimen, it is important to determine any pre-existing chronic pain and the use of long term analgesia. Pain assessment should be undertaken verbally. Unless the patient's age and cognitive status makes it impossible, this is the principal method[10] . These pain assessment methods give numerical values which are on a continuous or interval scale.

The various ways to the measurement of pain consists of

- verbal and numeric self-rating scales,
- behavioural observation scales and
- physiological responses.

The patient's self-report provides the most valid measure of the experience as pain is subjective. Verbal rating scales (VRS), visual analogue scales (VAS) , numerical rating scales (NRS) have been used to measure pain. They provide simple, easy, efficient and minimally intrusive measures of pain intensity.

An ideal tool for assessing pain :

- should be sensitive and free from bias,
- should be absolute ; rather than relative scales,
- must give accurate and reliable information,
- it should distinguish between pain, unpleasantness and emotion,

- it must assess experimental and clinical pain,
- it must estimate confidence of predictions.

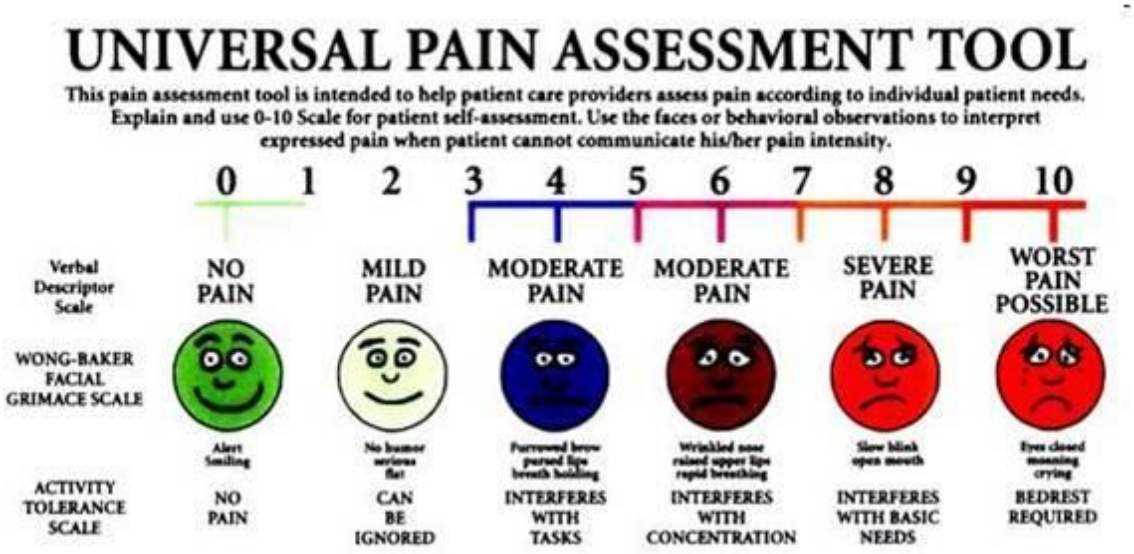
VERBAL RATING SCALES :

The verbal rating scales consist of a list of adjectives describing the different levels of pain intensity. It includes adjectives that reflect the extremes of pain ; from 'no pain' to 'extremely intense pain'. It must also have describing words to measure gradations of pain intensity. The patients are asked to select the phrase that best tells their level of pain. The commonly used scale is a 4 point scale. no pain = 0, mild pain = 1, moderate pain = 2 or severe pain = 3. VRSs are usually valid, easy to administer, score and comprehend. They are related significantly and positively to other measures of pain intensity.

NUMERICAL RATING SCALES :

The patient is asked to rate the pain from 0 to 10 or from 0 to 100. They only provide a verbal response which is then documented.

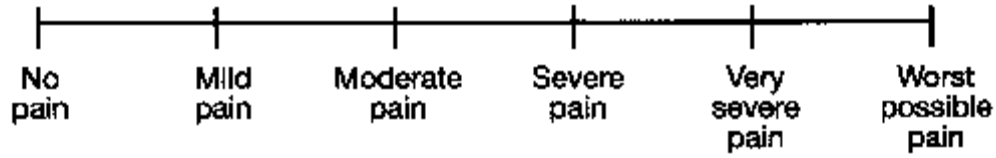
NRS are valid, easy to administer and score. It also demonstrates positive and significant correlations with other measures of pain intensity. It can be used in the elderly and in those with motor problems. The only drawback is that it assesses only pain intensity.



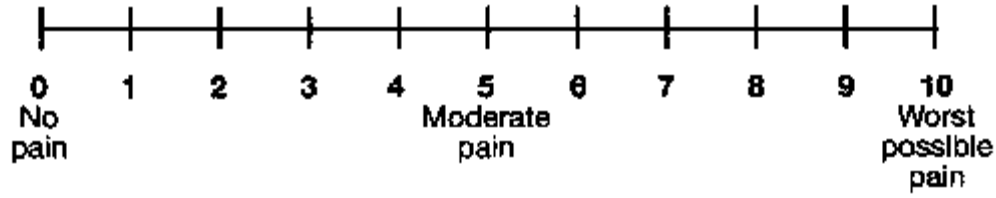
VISUAL ANALOG SCALE :

The visual analog score used for pain is a unidimensional measure of pain intensity. It is a continuous scale which comprises of a horizontal or a vertical line[11]. It is usually 10 centimeters or (100 mm) in length. The visual analog scale is a single-item scale. For the measurement of pain intensity, the scale is anchored by “no pain” (which is a score of 0) and “worst imaginable pain”(which is a score of 100). It is self- completed by the respondent. Using a scale, the score is determined by measuring the distance in (mm) on the 10-cm line. A higher score indicates a greater pain intensity. It provides a simple, very efficient and non-invasive method for pain measurement.

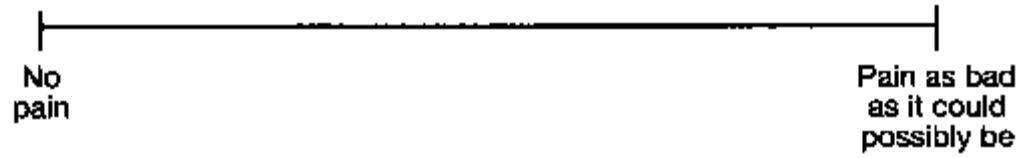
Simple Descriptive Pain Intensity Scale[1]



0–10 Numeric Pain Intensity Scale[1]



Visual Analog Scale (VAS)[2]



[1]If used as a graphic rating scale, a 10 cm baseline is recommended.
[2]A 10-cm baseline is recommended for VAS scales.

REVIEW OF LITERATURE

- Minai et al 2003

The aim of this randomized study was to correlate the analgesic effects of Morphine and Nalbuphine in patients undergoing total abdominal hysterectomies[12].

Fifty patients were part of the study. All the patients were given 7.5 mg of Midazolam orally as premedication.

Group A were given Morphine 0.1 mg/kg and Group B were given Nalbuphine 0.2 mg/kg. Anaesthesia was induced with Thiopentone 4mg/kg and 0.1 mg/kg Pancuronium was given for muscle relaxation. N2O : O2 – 66% : 33% and Halothane 0.5- 1% was used for maintenance. If signs of insufficient analgesia were present, supplemental doses of the study drug were given. The analgesic requirements and side effects were noted. The verbal category scale was used for assessing postoperative analgesia requirement.

Hemodynamic variables showed no significant difference between the groups. 4 of them required intraoperative analgesic supplements in the Nalbuphine group while it was 12 in the Morphine group. 5 of them in Morphine group had pain at reversal while none had pain in Nalbuphine group. The interval between the last intraoperative and the 1st postoperative dose was greater in the Morphine group. ($p < 0.05$). 5 in Morphine group and only 1 in Nalbuphine group had nausea and vomiting.

It was concluded that Nalbuphine provided better analgesia and hemodynamic stability with a lesser occurrence of nausea and vomitting when compared to Morphine. Also, Nalbuphine had a significantly longer duration of analgesia.

- Siddiqui et al 2007

This study was done to see the analgesic effects of Nalbuphine with Tramadol with the total intravenous anaesthesia technique[13]. In this study, a total of seventy patients were studied . All of them were monitored throughout the procedure, which consisted of heart rate (HR), non invasive blood pressure (B.P), ECG and oxygen saturation.

Group A - Inj.Tramadol 1.5 mg/kg iv after induction

Group B - Inj.Nalbuphine 0.1mg/kg iv after induction The patients were allowed to breathe spontaneously after the termination of action of Succinylcholine.

There was no statistical significant difference on comparing the demographic values. The variables such as systolic (SBP) and Diastolic blood pressure(DBP), Mean arterial pressure (MAP), Heart rate and oxygen saturation did not show any statistical significance. There was a statistically significant difference in the recovery profile. Sedation was more in Tramadol group. The pain score was evaluated by using the visual analog score. The incidence of pain was more in the Tramadol group.

It was concluded from the study that Nalbuphine had an early recovery postoperatively with better pain control and hemodynamic stability.

- Kenan et al 2007

This study was done to compare the analgesic effects of Tramadol and Lornoxicam on postoperative pain in patients, who underwent percutaneous nephrolithotomy[14].

Sixty patients were categorized into 3 groups, namely, Tramadol group, Lornoxicam group and Normal Saline (NS) group. Tramadol group were given 100 mg iv ; Lornoxicam group were given 8 mg iv ; and Normal Saline group were given 2 ml iv, ten minutes before induction. Anaesthesia was then induced with Inj.Fentanyl 1mcg/kg and Thiopentone sodium. Muscle relaxation was done with Inj.Vecuronium 0.1 mg/kg. O2: N20 – 50% : 50 % was used along with Desflurane 4-6% for maintenance. Mean blood pressure, heart rate, SpO2 were recorded before induction and also in the postoperative period.

Visual analog score, time to first analgesic, and the patient satisfaction scores were also documented in the postoperative pereriod.

The mean VAS score were significantly low in the Tramadol group ($p < 0.05$), when compared to NS group at 15, 30 mins and 1,2,4 hours. It was also lower in the Tramadol group at 1 hour after surgery, when compared with Lornoxicam group ($p < 0.05$). When compared to the Lornoxicam group, the time to 1st analgesic was longer in the Tramadol group. ($p < 0.05$). It was

concluded that both Tramadol and Lornoxicam were equally effective than normal saline, for postoperative pain control.

The analgesic efficacy of Tramadol was similar to Lornoxicam. At 1 hour, Tramadol was found to be more effective in patients undergoing percutaneous nephrolithotomy.

- Ouaki et al 2007

The aim of this trial was to compare the analgesic efficacy of intravenous continuous infusion of Nalbuphine and Tramadol given in equipotent doses[15]. The study was done in children aged 1 to 10 years, who were to undergo laparoscopic surgery under general anaesthesia. There was random allocation of children into two groups.

Nalbuphine group : (0.2 mg/kg, then infusion 0.8 mg/kg/24hrs , and bolus 0.1 mg/kg).

Tramadol group : (2 mg/kg , then infusion 8 mg/kg/24 hrs and bolus 1 mg/kg).

The pain score(CHIPPS), respiratory rate, heart rate, SpO2, mean arterial pressure, sedation, bolus requirements and side effects were recorded at regular intervals.

CHIPPS, hemodynamic and respiratory parameters were comparable in both the groups. The respirstory rate was lower in Nalbuphine group and Spo2 was lower, although it was not significant(p = 0.06 and 0.09). There was an

earlier requirement of a second bolus dose in Tramadol group (p = 0.02). Sedation was also found to be less in Tramadol group. (p = 0.01).

It was concluded that Tramadol appeared to be atleast as efficient as Nalbuphine in treating post-operative pain.

- Van den berg et al 2011

This study was done to compare the analgesic efficacy and the safety profile of Tramadol, Nalbuphine and Pethidine given in equipotent doses with a placebo (saline 0.02 ml/kg) given during induction[16].

This study was done in 152 ASA I children and young adults who came for adeno-tonsillectomy. Drugs used for premedication (Temazepam and Diclofenac), and drugs used for induction(Thiopentone) and maintenance were also the same.

The heart rate (HR) and systolic blood pressure (SBP) were monitored. Esmolol,, 2.0 mg/kg intravenously was used for treating any increase in HR or SBP >33% of baseline.

Placebo group required more amount of Esmolol. The Tramadol requirement in recovery was reduced (P<0.05). Both Pethidine and Nalbuphine caused a significant reduction in the requirement of Esmolol.

There was also a decrease in the need for treatment with opioids during recovery in the two groups(P<0.005 each). At the end of anesthesia, only Pethidine caused a delay in the recovery of spontaneous respiration. The other recovery variables were found to be similar. The restlessness–pain scores were reduced by all the three drugs.

It was concluded that Nalbuphine and Pethidine provided better analgesia than Tramadol. The safety profile of Nalbuphine and Tramadol was found to be more than Pethidine.

- Shaila et al 2013

This study was done to evaluate the analgesic effects of intravenous Nalbuphine and intravenous Tramadol on postoperative pain[17].

Eighty patients undergoing elective surgery under general anaesthesia were randomly divided into two groups of forty each.

Patients were premedicated with Diazepam 0.15mg/kg orally at night before and in the morning. After shifting to the operating room, Midazolam 0.02mg/kg and Fentanyl 2mcg/kg were given. Patients were induced with Propofol 2-2.5mg/kg and muscle relaxation was done with Vecuronium 0.1mg/kg. O2 : N2O mixture with Isoflurane was given. After the end of procedure, they were reversed and extubated. They were allocated into two groups.

When the pain score was more than three, Group A was given Inj.Nalbuphine (0.2mg/kg iv) postoperatively and Group B was given Inj.Tramadol (1mg/kg iv) postoperatively. The percentage of pain relief in Nalbuphine group was highly significant as compared to Tramadol group at 30 mins. Mean VAS in Nalbuphine group was 0.72+/-0.64 and mean VAS in Tramadol group was 1.72 +/- 0.75 at 30 mins. Pain relief was also significant at the end of 1,2, 4, 6, 8 hours.

Tramadol group had a significant incidence of nausea and vomiting. Drowsiness (12.5%) was more in Nalbuphine group when compared to Tramadol.

It was concluded that Nalbuphine appears to be an effective and safe analgesic for postoperative pain relief than Tramadol in equianalgesic doses. Nalbuphine was found to have minimum circulatory effects, provided good sedation and also a lower incidence of nausea and vomiting. They also told that its use in the postoperative period can attenuate the mu- opioid related side effects, and a ceiling respiratory depression

- Shiv akshat et al 2014

This study was done to compare the analgesic efficacy and side effects of Nalbuphine and Morphine in patients undergoing gynecological surgeries[18]. VAS score was the primary outcome. Secondary outcomes were the requirement of rescue analgesics and side effects. Sixty patients were included in this study.

Group M (Morphine) and group N (Nalbuphine). Drug solution to be used as PCA was prepared by dissolving 20mg Nalbuphine/Morphine in 20 ml Normal saline.

Induction was done with 0.1ml/kg of the solution of unknown opioid and a sleep dose of Propofol. Vecuronium 0.1 mg/kg was given for muscle relaxation. O2, N2O, Isoflurane were used for maintenance of anaestheisa. After extubation, they were shifted to the post-anaesthesia care unit.

The need for intraoperative analgesia in Nalbuphine group was significantly more. The hemodynamic parameters were comparable between the two groups in both the intraoperative and the postoperative period. There was no significant difference in the occurrence of side effects among the two groups.

It was concluded that both drugs provided similar postoperative analgesia with a similar hemodynamic and side effect profile. However, Nalbuphine was found to be less effective in the intra-operative period.

- Ananda et al 2015

The aim of this prospective- randomized, double-blind study was to compare the analgesic efficacy of intravenous Nalbuphine and intravenous Morphine in patients undergoing total abdominal hysterectomy[19].

Duration of analgesia in the post-operative period was the primary outcome. Intra-operative hemodynamics and the occurrence of side effects were the secondary outcomes. 30 patients were selected. They were randomly alloted into 2 groups. All the patients underwent general anaesthesia. After shifting inside OT, monitors were connected and peripheral iv line started. They were then preoxygenated for 3 mins.

Group N –received inj.Nalbuphine 0.2 mg/kg iv and Group M – received inj.Morphine 0.1 mg/kg iv. Induction was done with 2 mg/kg Propofol iv and neuromuscular blockade was attained with Inj.Vecuronium 0.1 mg/kg.patients were maintained with N2O ; O2 – 66% ; 33% and 1MAC Isoflurane.

Hemodynamic parameters were monitored intraoperatively every 5 mins and in the post-operative period for every 15 mins. The duration of analgesia was about 255+/- 43.75 mins in Morphine group and it was 437 +/- 63.87 in Nalbuphine group. So there was an early usage of rescue analgesic (75 mg of Diclofenac) in Morphine group, which was statistically significant ($p<0.001$).

The heart rate was less in Morphine group when compared to Nalbuphine group. ($p< 0.005$). The systolic and diastolic blood pressures were also low in Nalbuphine group. Patients in Nalbuphine group were sedated even after 30 mins following extubation, when compared to Morphine.

Hence it was concluded that Nalbuphine is an effective analgesic with less circulatory effects, less respiratory depression and produced good sedation.

- Solanki et al 2015

The study was to compare the analgesic efficacy of intravenous Nalbuphine and Tramadol on postoperative pain in orthopaedic surgeries[20].

Eighty patients, belonging to ASA PS 1 & 2 were studied.

Premedication was done with Tab.Diazepam 5mg given orally in the morning before surgery. The surgery was done under general/ regional anaesthesia. Then the patients were assessed for postoperative pain.

Nalbuphine group – Inj.Nalbuphine 0.15 mg/kg iv 8 hours apart and Tramadol group – Inj.Tramadol 2 mg/kg iv 8 hours apart was given. The parameters measured were VAS score, BP, PR, RR, SpO2, side effects of drugs and the requirement of rescue analgesic.

The results and observations were derived by applying chi square test and students T test. A p value< 0.05 was considered as statistically significant.

The Nalbuphine group had significantly higher average sedation scores ($p < 0.0001$). Rescue analgesic requirement was more in the Tramadol group. Tramadol group had a greater incidence of nausea and vomiting. There was some degree of respiratory depression in Nalbuphine group. There was a greater amount of hemodynamic stability in Nalbuphine group ($p < 0.005$). With successive doses, the duration of analgesia became significant and it was longer in Nalbuphine group. There was no occurrence of hypotension or bradycardia in both the groups.

It was concluded that Nalbuphine produced better pain relief and hemodynamic stability when compared to Tramadol in the post-operative period.

METHODS

The study, **"A Prospective, randomized study comparing the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy".** was duly submitted before the ethical committee of our institution and the ethical committee approval was obtained. The study was done on 60 patients coming for percutaneous nephrolithotomy, the procedure being done under general anaesthesia.

INCLUSION CRITERIA:

- Age : 20 -60 years
- Sex : both
- Weight : BMI < 30 Kg/m2
- ASA : I & II
- Surgery : Elective
- Mallampatti scores : I & II
- Who has given valid informed consent.

EXCLUSION CRITERIA:

- Patients not satisfying inclusion criteria.
- Patients posted for emergency surgery
- Patients with difficult airway
- Patients with respiratory or cardiac disease
- Lack of written informed consent
- H/O seizures and any neurological deficit or on psychotropic drugs
- H/O tolerance, dependence or allergy to opioids
- H/O chronic alcohol consumption
- Patients with diminished mental competence, deafness and visual disturbances.

The patients who satisfied the inclusion criteria were explained about the nature of procedure, tests, advantages and side effects in an elaborate manner. A written informed consent was then obtained from the patients. Then they were assessed and investigated. Age, height, weight, body mass index of the patients were noted down. Various vital parameters like blood pressure, heart rate, respiratory rate, oxygen saturation were also noted. Investigations included a complete blood count, blood sugar, urea, creatinine, bleeding time, clotting time, liver function tests, ecg and chest x-ray. Then examination of the various systems and airway assessment was done. Explanation about the visual analog score (VAS) was given to all patients. They were told that 0 represented “no pain” and 10 represented “ worst possible pain” on the grading scale.

MATERIALS

DRUGS :

- Inj. Glycopyrrolate
- Inj.Fentanyl
- Inj.Thiopentone sodium
- Inj,Atracurium
- Inj.Neostigmine
- Inj.Nalbuphine
- Inj.Tramadol
- All the emergency drugs were kept ready.

INTRAVENOUS FLUIDS :

- Normal saline (NS)
- Ringer lactate (RL)

MONITORS :

- NIBP
- ECG
- SpO2
- EtCO2
- Temperature
- Urine output

The patient was shifted into the operating room. Monitors like non-invasive blood pressure, ECG, pulse oximetry were connected. The baseline vitals like the diastolic and systolic blood pressure, heart rate, SpO2 were recorded. Then an intravenous access with a 18G intravenous cannula was obtained. Premedication was done with inj.glycopyrrolate 0.2 mg and inj.fentanyl 2mcg/kg. The patient was then preoxygenated with a 100 % O2 for 5 minutes. Induction was done with inj.Thiopentone and muscle relaxation was obtained with inj.Atracurium. The patient was then ventilated with a N2O : O2 in the ratio of 50% : 50% along with desflurane 6% for a time interval of 3 minutes. Endotracheal intubation was then done with the cuffed endotracheal tube of appropriate size. Maintenance of anaesthesia was attained with N2O :O2 in the ratio of 50 % : 50 % along with desflurane 3 -6%.

Towards the end of the surgery the patients were randomized into 2 groups,

GROUP A(Nalbuphine) : received a bolus dose of 0.2mg/kg 30 mins before extubation.

GROUP B (Tramadol) : received a bolus dose of 1mg/kg 30 mins before extubation.

After the end of the surgery, reversal was done with inj.glcopyrrolate 0.01 mg/kg and inj.neostigmine 0.05 mg/kg and extubated after thorough oral suctioning. Vitals and visual analog score were then monitored immediately and also post operatively at regular intervals in the post-operative ward. When the vas score was greater than 3, the patients were given rescue analgesic, inj.diclofenac 75 mg intramuscularly.

PARAMETERS MONITORED

- Age, sex, weight, height, body mass index.

PRIMARY OUTCOME MEASURES:

- Post-operative visual analog score and
- Systolic blood pressure(SBP), diastolic blood pressure(DBP), mean arterial pressure(MAP), heart rate(HR), respiratory rate(RR) and oxygen saturation(Spo2) were measured at baseline and at intervals of 1,5 15,30 mins and 1,2 4,6,8,10 hours postoperatively.

SECONDARY OUTCOME MEASURES :

- Post-operative rescue analgesic initiation time
- Side effects and any other complications.

The time interval between the administration of the study drug and the time when the VAS score becomes greater than 3 is known as the rescue analgesic initiation time. Inj.diclofenac im was used as the rescue analgesic.

OBSERVATIONS AND ANALYSIS :

The study is a prospective, randomized study comparing the analgesic effects of intravenous nalbuphine with intravenous tramadol on post-operative pain and post-operative analgesic requirements for patients undergoing percutaneous nephrolithotomy.

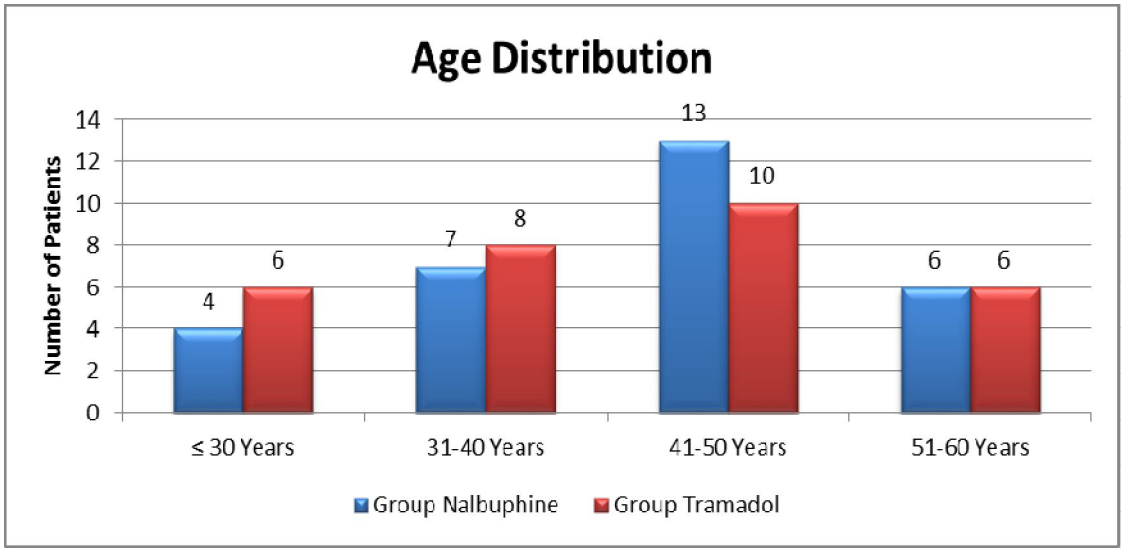
GROUP A (NALBUPHINE) : received a bolus dose of 0.2 mg/kg nalbuphine iv, 30 minutes before extubation

GROUP B (TRAMADOL) : received a bolus dose of 1 mg/kg tramadol iv, 30 minutes before extubation.

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t test. Categorical variables were analysed with Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 16 and Microsoft Excel 2007.

DEMOGRAPHIC PROFILE

AGE :



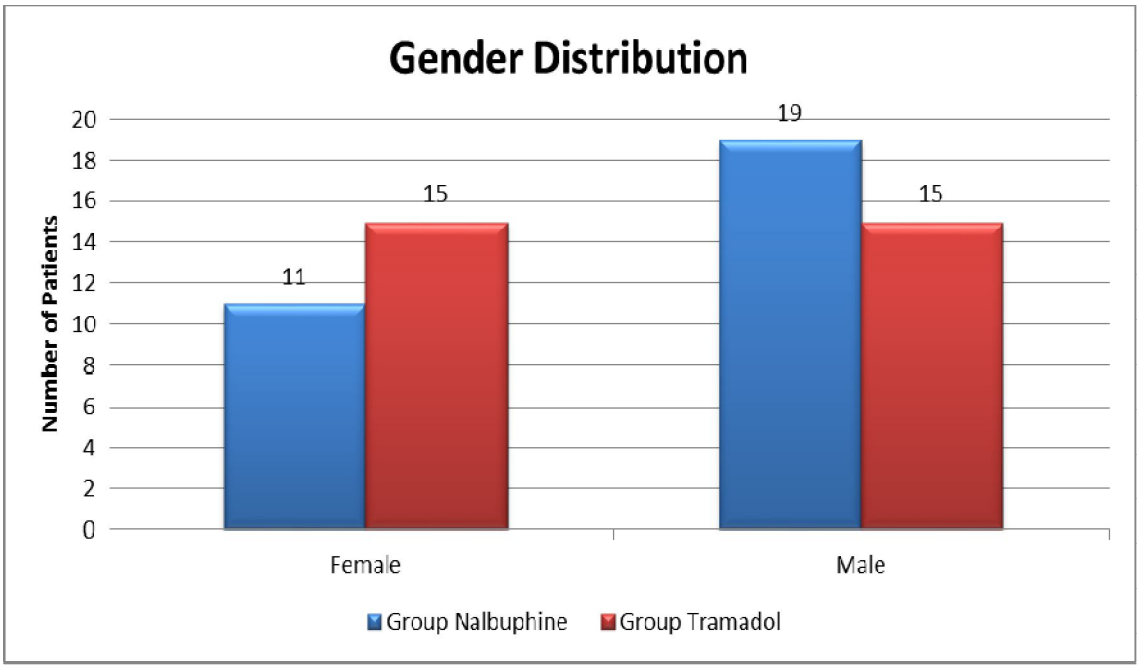
Age Distribution	Group Nalbuphine	%	Group Tramadol	%
≤ 30 Years	4	13.33	6	20.00
31-40 Years	7	23.33	8	26.67
41-50 Years	13	43.33	10	33.33
51-60 Years	6	20.00	6	20.00
Total	30	100	30	100

Age Distribution	Group Nalbuphine	Group Tramadol
N	30	30
Mean	43.33	41.37
SD	9.90	10.24
P value Unpaired t Test		0.452561

Majority of the Nalbuphine Group patients belonged to the 41-50 Years age class interval (n=13, 43.33%) with a mean age of 43.33 years. In the Tramadol group patients, majority belonged to the 41-50 years age class interval (n=10, 33.33%) with a mean age of 41.37 years. The association between the intervention groups and age distribution is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

GENDER :

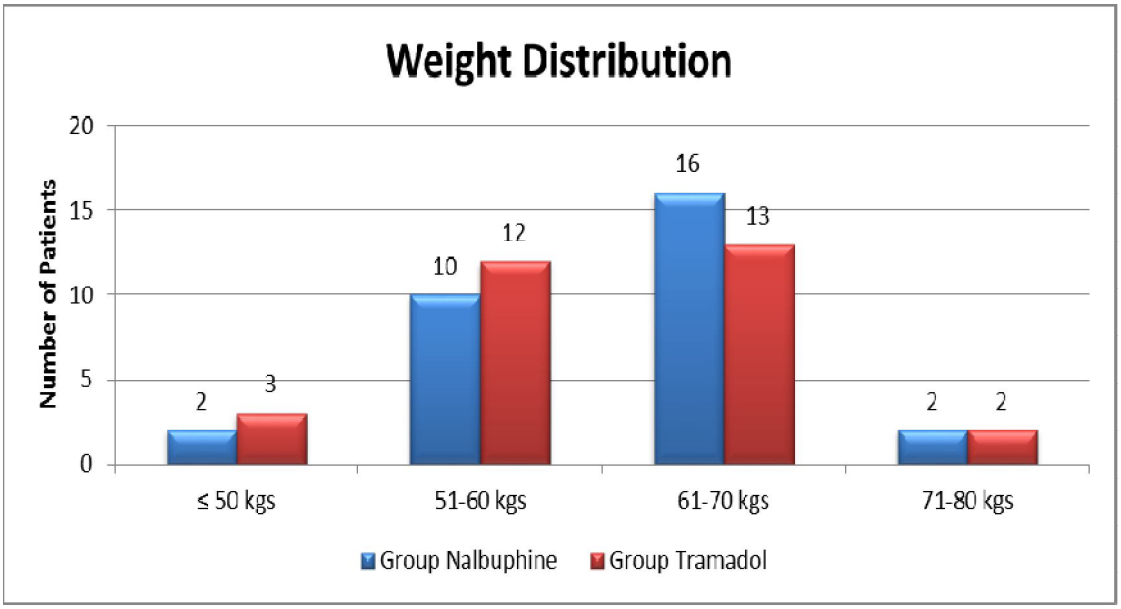
The two groups showed the following gender distribution.



Gender Distribution	Group Nalbuphine	%	Group Tramadol	%	P value Chi Squared Test
Female	11	36.67	15	50.00	0.2974
Male	19	63.33	15	50.00	
Total	30	100	30	100	

Majority of the Nalbuphine Group patients belonged to the male gender group (n=19, 63.33%). In the Tramadol group patients, there was equal distribution among the male gender and female gender groups (n=15, 50%). The association between the intervention groups and gender distribution is considered to be not statistically significant since $p > 0.05$ as per chi squared test.

WEIGHT :

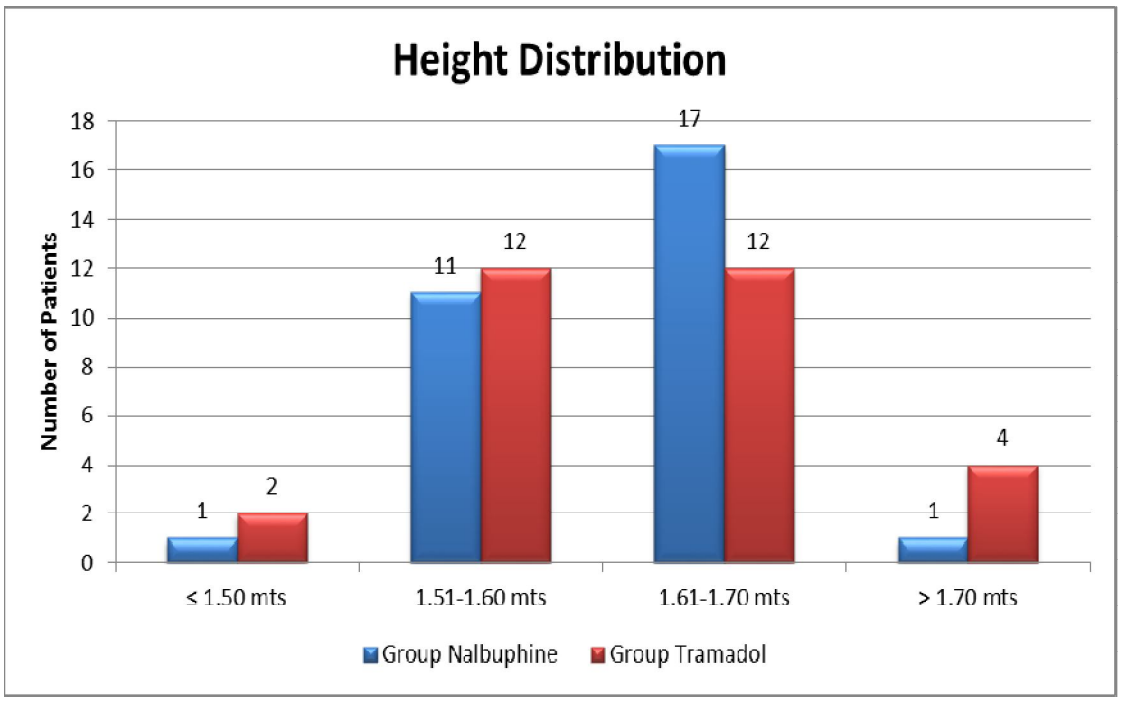


Weight Distribution	Group Nalbuphine	%	Group Tramadol	%
≤ 50 kgs	2	6.67	3	10.00
51-60 kgs	10	33.33	12	40.00
61-70 kgs	16	53.33	13	43.33
71-80 kgs	2	6.67	2	6.67
Total	30	100	30	100

Weight Distribution	Group Nalbuphine	Group Tramadol
N	30	30
Mean	61.63	60.77
SD	6.65	7.11
P value Unpaired t Test		0.627669

Majority of the Nalbuphine Group patients belonged to the 61-70 kgs weight class interval (n=16, 53.33%) with a mean weight of 61.63 kgs. In the Tramadol group patients, majority belonged to the 61-70 kgs weight class interval (n=13, 43.33%) with a mean weight of 60.77 kgs. The association between the intervention groups and weight distribution is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

HEIGHT :

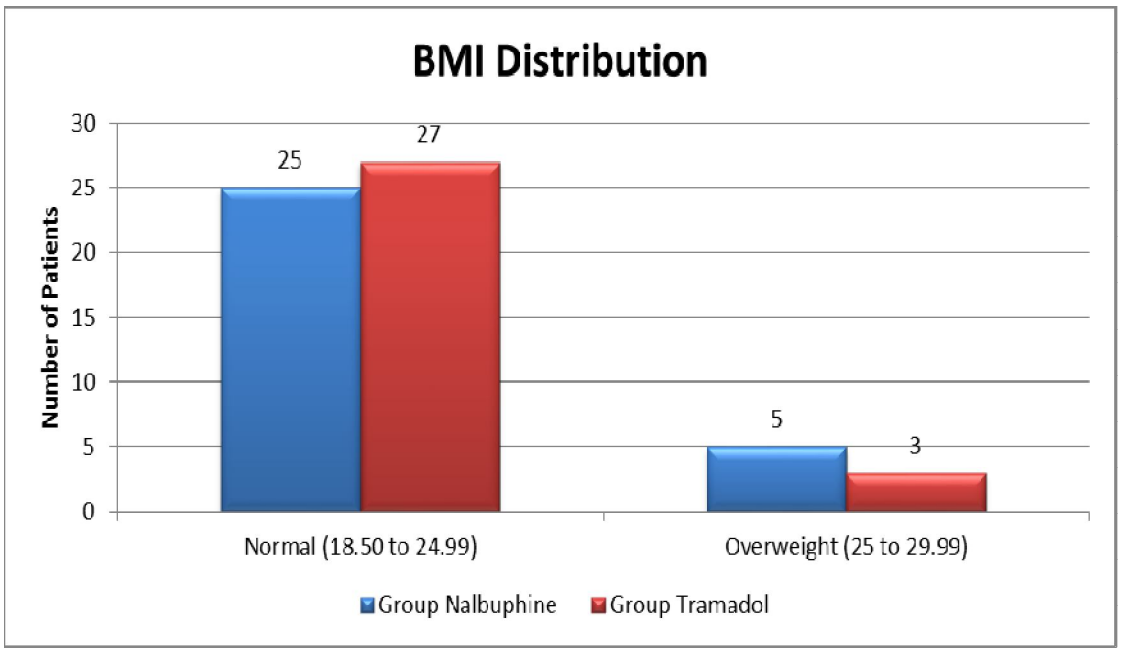


Height Distribution	Group Nalbuphine	%	Group Tramadol	%
≤ 1.50 mts	1	3.33	2	6.67
1.51-1.60 mts	11	36.67	12	40.00
1.61-1.70 mts	17	56.67	12	40.00
> 1.70 mts	1	3.33	4	13.33
Total	30	100	30	100

Height Distribution	Group Nalbuphine	Group Tramadol
N	30	30
Mean	1.61	1.62
SD	0.07	0.08
P value Unpaired t Test		0.631409

Majority of the Nalbuphine Group patients belonged to the 1.61-1.70 meters height class interval (n=17, 56.67%) with a mean height of 1.61 meters. In the Tramadol group patients, majority belonged to the 1.61-1.70 meters height class interval (n=12, 40%) with a mean height of 1.62 meters. The association between the intervention groups and height distribution is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

BODY MASS INDEX :



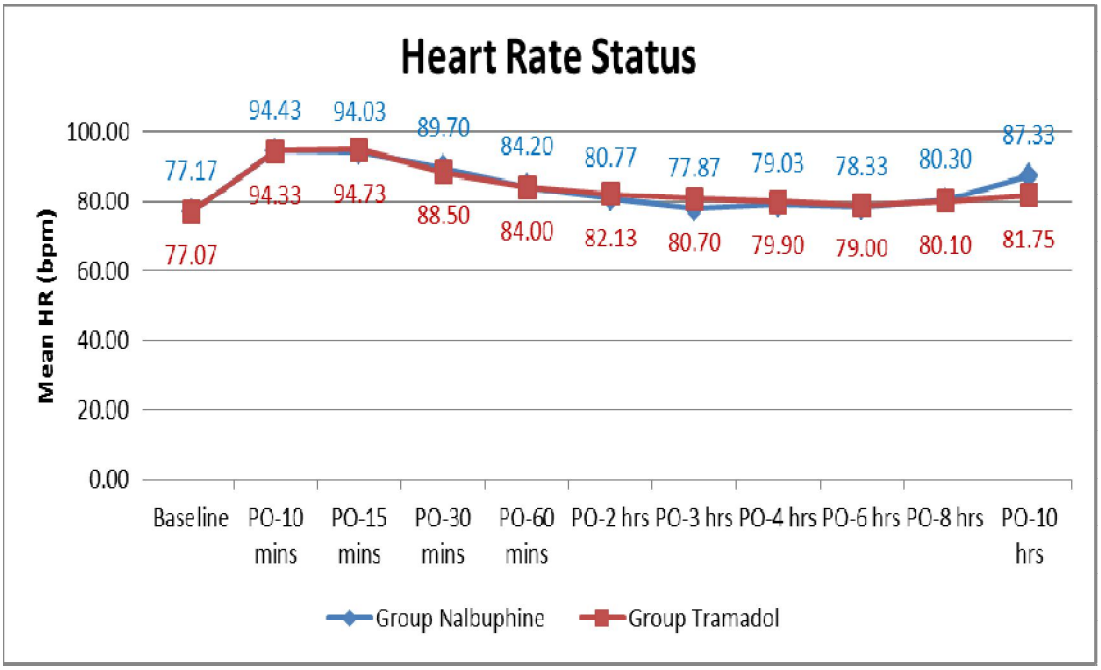
BMI Distribution	Group Nalbuphine	%	Group Tramadol	%
Underweight (≤ 18.49)	0	0.00	0	0.00
Normal (18.50 to 24.99)	25	83.33	27	90.00
Overweight (25 to 29.99)	5	16.67	3	10.00
Obese	0	0.00	0	0.00
Total	30	100	30	100

BMI Distribution	Group Nalbuphine	Group Tramadol
N	30	30
Mean	23.81	23.18
SD	1.35	1.52
P value Unpaired t Test		0.09453

Majority of the Nalbuphine Group patients belonged to the normal BMI class interval (n=25, 83.33%) with a mean BMI of 23.81. In the Tramadol group patients, majority belonged to the normal BMI class interval (n=27, 90%) with a mean BMI of 23.18. The association between the intervention groups and BMI distribution is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

VITALS :

HEART RATE

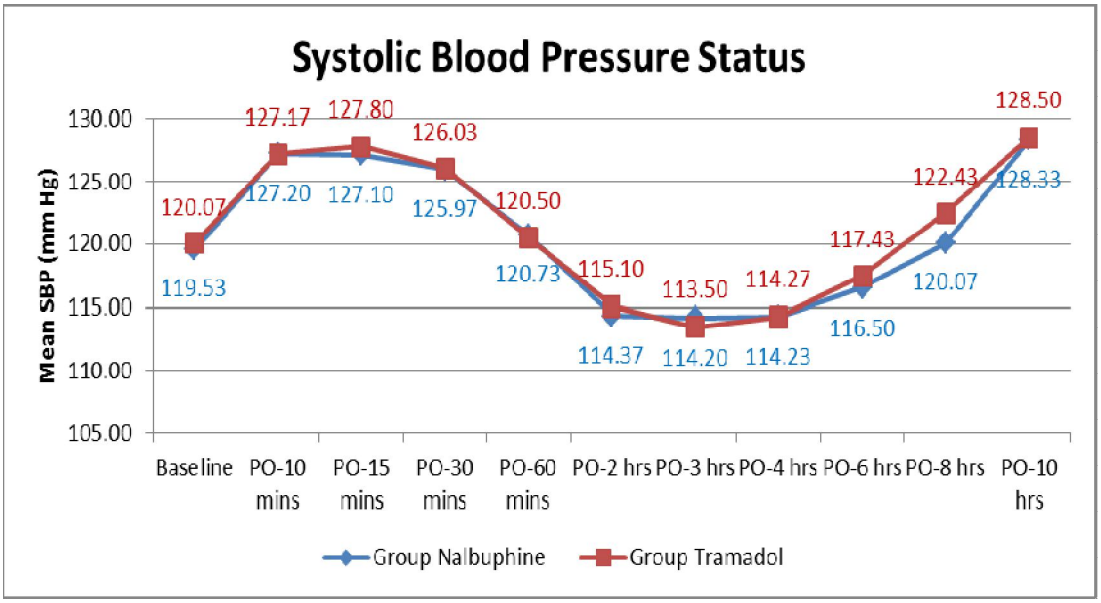


Heart Rate Status		Baseline	PO-10 mins	PO-15 mins	PO-30 mins	PO-60 mins
Group Nalbuphine	N	30	30	30	30	30
	Mean	77.17	94.43	94.03	89.70	84.20
	SD	8.28	9.46	8.50	7.32	7.12
Group Tramadol	N	30	30	30	30	30
	Mean	77.07	94.33	94.73	88.50	84.00
	SD	7.41	7.28	6.67	6.85	5.73
P value Unpaired t Test		0.9609	0.9636	0.7240	0.5148	0.9050

Heart Rate Status		PO-2 hrs	PO-3 hrs	PO-4 hrs	PO-6 hrs	PO-8 hrs	PO-10 hrs
Group Nalbuphine	N	30	30	30	30	30	9
	Mean	80.77	77.87	79.03	78.33	80.30	87.33
	SD	6.56	6.07	5.46	6.33	6.73	4.33
Group Tramadol	N	30	30	30	30	30	4
	Mean	82.13	80.70	79.90	79.00	80.10	81.75
	SD	5.24	5.21	5.92	6.96	7.05	2.75
P value Unpaired t Test		0.3766	0.1472	0.2480	0.1293	0.4109	0.0705

Majority of the Nalbuphine Group patients had mean heart rate ranging from 77.17 bpm at baseline to 87.33 bpm at 10 hours postoperatively. Similarly majority of the Tramadol Group patients had mean heart rate ranging from 77.07 bpm at baseline to 81.75 bpm at 10 hours postoperatively. The association between the intervention groups and heart rate is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

SYSTOLIC BLOOD PRESSURE :

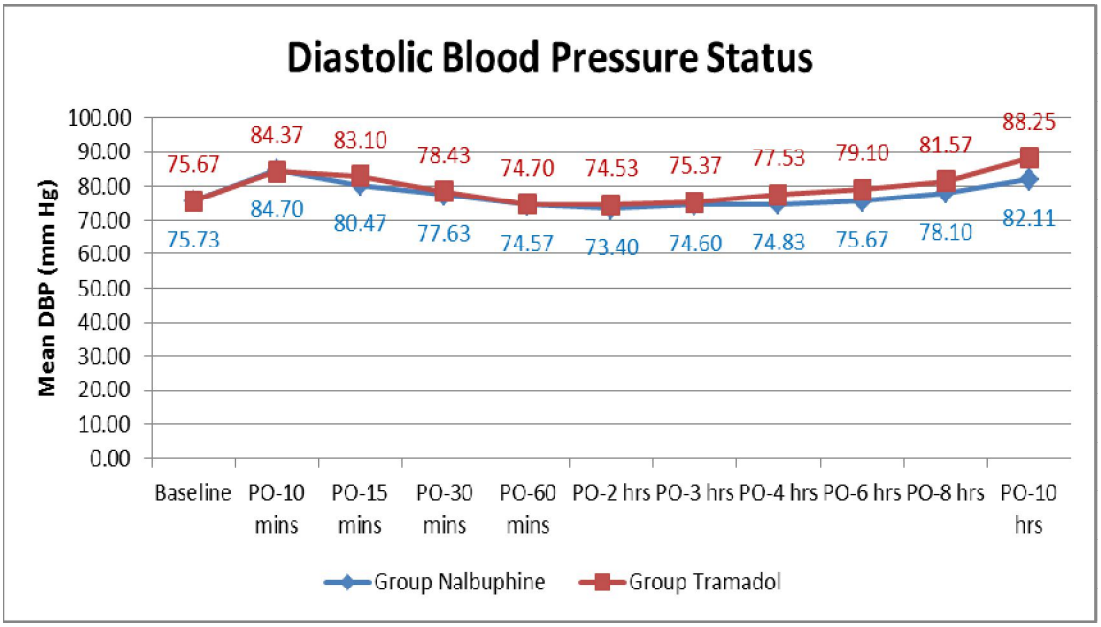


Systolic Blood Pressure Status		Baseline	PO-10 mins	PO-15 mins	PO-30 mins	PO-60 mins
Group Nalbuphine	N	30	30	30	30	30
	Mean	119.53	127.20	127.10	125.97	120.73
	SD	7.07	7.52	7.09	7.25	5.65
Group Tramadol	N	30	30	30	30	30
	Mean	120.07	127.17	127.80	126.03	120.50
	SD	6.52	6.24	6.60	6.82	6.14
P value Unpaired t Test		0.7625	0.9852	0.6937	0.9709	0.8788

Systolic Blood Pressure Status		PO-2 hrs	PO-3 hrs	PO-4 hrs	PO-6 hrs	PO-8 hrs	PO-10 hrs
Group Nalbuphine	N	30	30	30	30	30	9
	Mean	114.37	114.20	114.23	116.50	120.07	128.33
	SD	5.26	4.94	5.36	3.94	5.35	5.66
Group Tramadol	N	30	30	30	30	30	4
	Mean	115.10	113.50	114.27	117.43	122.43	128.50
	SD	5.97	4.90	4.69	4.99	4.25	0.58
P value Unpaired t Test		0.6158	0.5835	0.9796	0.4246	0.0630	0.9324

Majority of the Nalbuphine Group patients had mean systolic blood pressure ranging from 114.37 mm Hg at baseline to 128,33 mm Hg at 10 hours postoperatively. Similarly majority of the Tramadol Group patients had mean systolic blood pressure ranging from 115.10 mm Hg at baseline to 128,50 mm Hg at 10 hours postoperatively. The association between the intervention groups and systolic blood pressure is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

DIASTOLIC BLOOD PRESSURE :

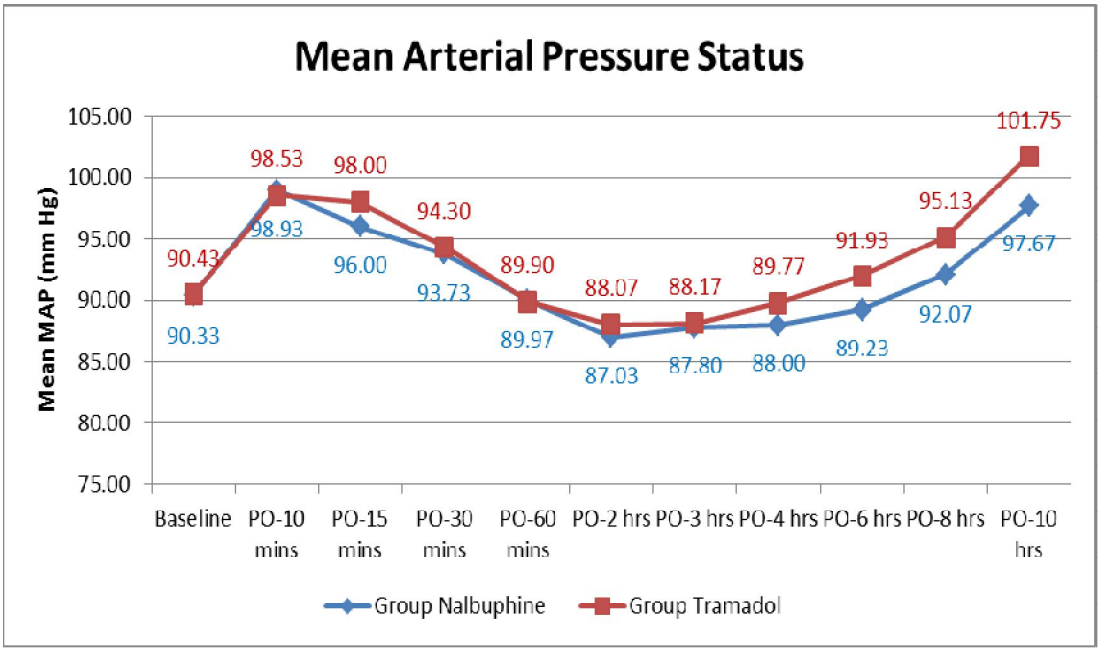


Diastolic Blood Pressure Status		Baseline	PO-10 mins	PO-15 mins	PO-30 mins	PO-60 mins
Group Nalbuphine	N	30	30	30	30	30
	Mean	75.73	84.70	80.47	77.63	74.57
	SD	7.18	7.24	6.34	4.68	4.30
Group Tramadol	N	30	30	30	30	30
	Mean	75.67	84.37	83.10	78.43	74.70
	SD	6.38	5.35	4.78	4.71	4.98
P value Unpaired t Test		0.9698	0.8400	0.0748	0.5119	0.9120

Diastolic Blood Pressure Status		PO-2 hrs	PO-3 hrs	PO-4 hrs	PO-6 hrs	PO-8 hrs	PO-10 hrs
Group Nalbuphine	N	30	30	30	30	30	9
	Mean	73.40	74.60	74.83	75.67	78.10	82.11
	SD	4.94	4.51	4.91	5.45	6.25	3.14
Group Tramadol	N	30	30	30	30	30	4
	Mean	74.53	75.37	77.53	79.10	81.57	88.25
	SD	5.32	5.14	5.40	5.04	4.12	2.22
P value Unpaired t Test		0.3958	0.5416	0.4473	0.3140	0.5144	0.0936

Majority of the Nalbuphine Group patients had mean diastolic blood pressure ranging from 75.73 mm Hg at baseline to 82.11 mm Hg at 10 hours postoperatively. Similarly majority of the Tramadol Group patients had mean diastolic blood pressure ranging from 75.67 mm Hg at baseline to 88.25 mm Hg at 10 hours postoperatively. The association between the intervention groups and diastolic blood pressure is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

MEAN ARTERIAL PRESSURE :

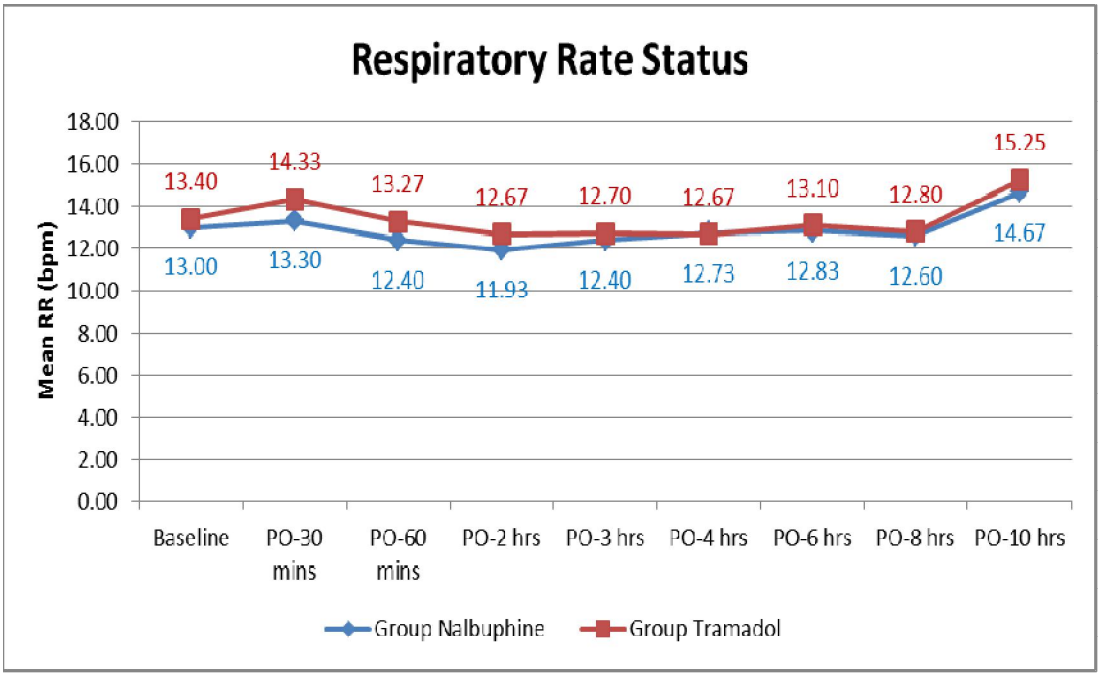


Mean Arterial Pressure Status		Baseline	PO-10 mins	PO-15 mins	PO-30 mins	PO-60 mins
Group Nalbuphine	N	30	30	30	30	30
	Mean	90.33	98.93	96.00	93.73	89.97
	SD	6.96	7.06	6.18	4.95	4.43
Group Tramadol	N	30	30	30	30	30
	Mean	90.43	98.53	98.00	94.30	89.90
	SD	6.35	5.17	5.01	5.17	4.87
P value Unpaired t Test		0.9538	0.8033	0.1741	0.6662	0.9560

Mean Arterial Pressure Status		PO-2 hrs	PO-3 hrs	PO-4 hrs	PO-6 hrs	PO-8 hrs	PO-10 hrs
Group Nalbuphine	N	30	30	30	30	30	9
	Mean	87.03	87.80	88.00	89.23	92.07	97.67
	SD	4.34	3.84	3.57	3.74	4.70	3.61
Group Tramadol	N	30	30	30	30	30	4
	Mean	88.07	88.17	89.77	91.93	95.13	101.75
	SD	4.64	4.60	4.60	4.59	3.89	1.71
P value Unpaired t Test		0.3768	0.7387	0.1023	0.3154	0.1180	0.2185

Majority of the Nalbuphine Group patients had mean arterial pressure ranging from 90.33 mm Hg at baseline to 97.67 mm Hg at 10 hours postoperatively. Similarly majority of the Tramadol Group patients had mean arterial pressure ranging from 90.43 mm Hg at baseline to 101.75 mm Hg at 10 hours postoperatively. The association between the intervention groups and mean arterial pressure is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

RESPIRATORY RATE :

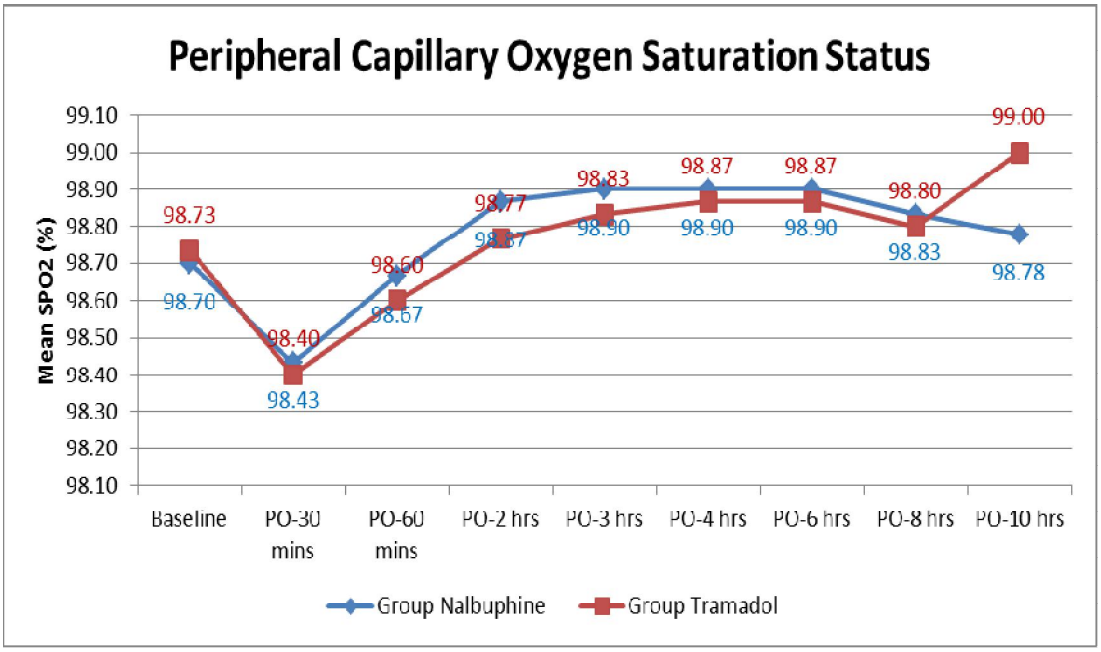


Respiratory Rate Status		Baseline	PO-30 mins	PO-60 mins	PO-2 hrs	PO-3 hrs
Group Nalbuphine	N	30	30	30	30	30
	Mean	13.00	13.30	12.40	11.93	12.40
	SD	1.20	1.42	0.72	0.74	1.00
Group Tramadol	N	30	30	30	30	30
	Mean	13.40	14.33	13.27	12.67	12.70
	SD	1.22	1.71	1.01	0.92	0.84
P value Unpaired t Test		0.2063	0.1136	0.2564	0.9713	0.2137

Respiratory Rate Status		PO-4 hrs	PO-6 hrs	PO-8 hrs	PO-10 hrs
Group Nalbuphine	N	30	30	30	9
	Mean	12.73	12.83	12.60	14.67
	SD	1.08	0.83	1.61	0.71
Group Tramadol	N	30	30	30	4
	Mean	12.67	13.10	12.80	15.25
	SD	1.03	1.06	1.16	0.50
P value Unpaired t Test		0.8075	0.2841	0.5829	0.1268

Majority of the Nalbuphine Group patients had mean respiratory rate ranging from 13 bpm at baseline to 14.67 bpm at 10 hours postoperatively. Similarly majority of the Tramadol Group patients had mean respiratory rate ranging from 13.40 bpm at baseline to 15.25 bpm at 10 hours postoperatively. The association between the intervention groups and respiratory rate is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

SpO2 :



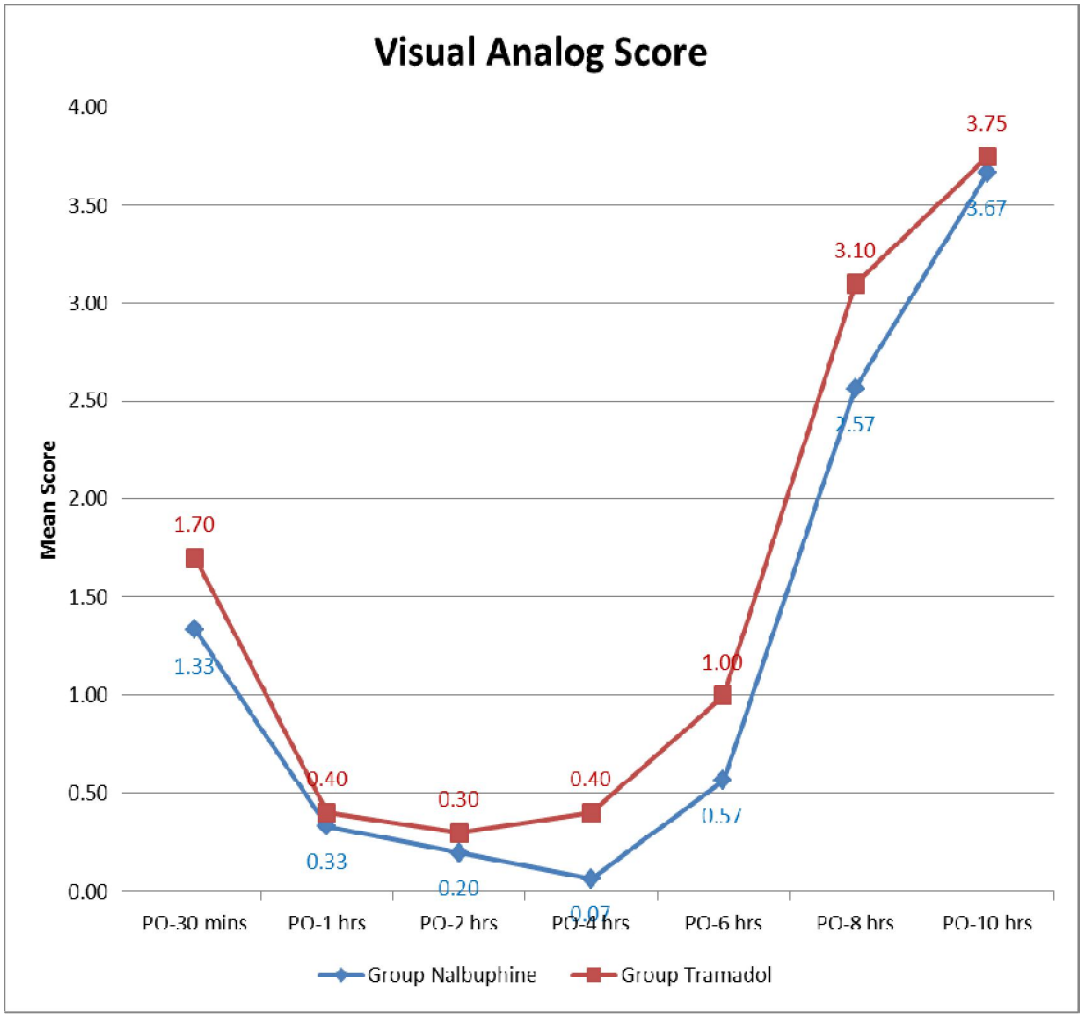
Peripheral Capillary Oxygen Saturation Status		Baseline	PO-30 mins	PO-60 mins	PO-2 hrs	PO-3 hrs
Group Nalbuphine	N	30	30	30	30	30
	Mean	98.70	98.43	98.67	98.87	98.90
	SD	0.47	0.57	0.48	0.35	0.31
Group Tramadol	N	30	30	30	30	30
	Mean	98.73	98.40	98.60	98.77	98.83
	SD	0.45	0.62	0.50	0.43	0.38
P value Unpaired t Test		0.7790	0.8291	0.5995	0.3253	0.4562

Peripheral Capillary Oxygen Saturation Status		PO-4 hrs	PO-6 hrs	PO-8 hrs	PO-10 hrs
Group Nalbuphine	N	30	30	30	9
	Mean	98.90	98.90	98.83	98.78
	SD	0.31	0.31	0.38	0.44
Group Tramadol	N	30	30	30	4
	Mean	98.87	98.87	98.80	99.00
	SD	0.35	0.35	0.41	0.00
P value Unpaired t Test		0.6936	0.6936	0.7438	0.1690

Majority of the Nalbuphine Group patients had Peripheral Capillary Oxygen Saturation ranging from 98.70 % at baseline to 98.78 % at 10 hours postoperatively. Similarly majority of the Tramadol Group patients had mean Peripheral Capillary Oxygen Saturation ranging from 98.73 % at baseline to 99 % at 10 hours postoperatively. The association between the intervention groups and Peripheral Capillary Oxygen Saturation is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

VISUAL ANALOG SCORE :

The postoperative pain scores in the two groups, which were analysed by the visual analog score, were as follows,



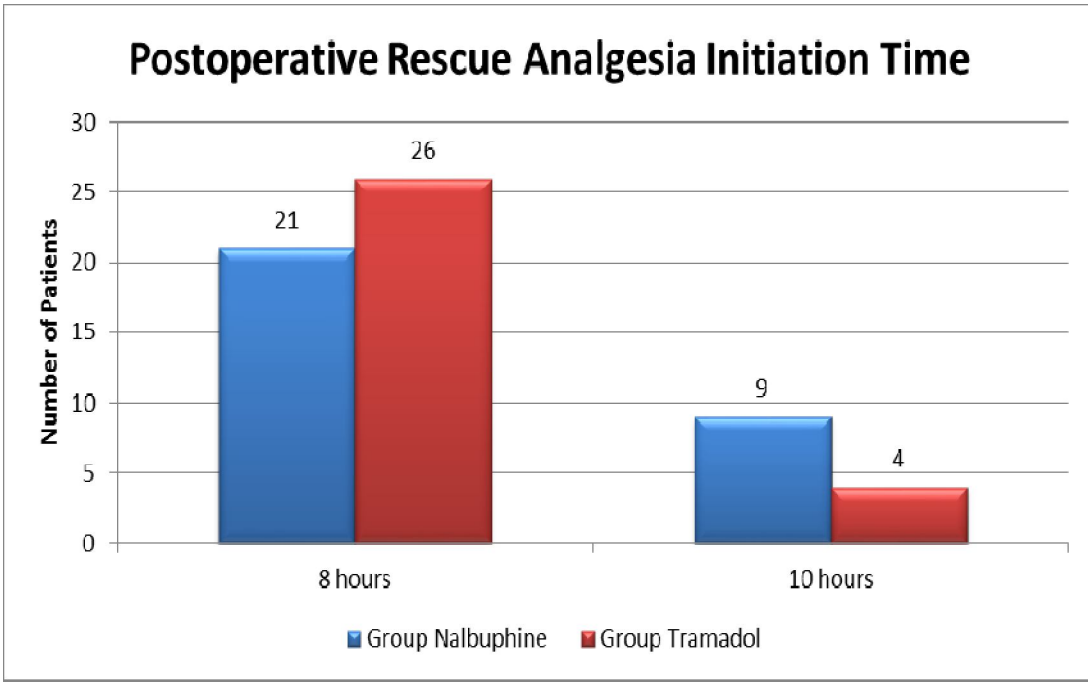
Visual Analog Score		PO-30 mins	PO-1 hrs	PO-2 hrs	PO-4 hrs	PO-6 hrs	PO-8 hrs	PO-10 hrs
Group Nalbuphine	N	30	30	30	30	30	30	9
	Mean	1.33	0.33	0.20	0.07	0.57	2.57	3.67
	SD	0.55	0.48	0.41	0.25	0.57	0.73	0.71
Group Tramadol	N	30	30	30	30	30	30	4
	Mean	1.70	0.40	0.30	0.40	1.00	3.10	3.75
	SD	0.60	0.50	0.47	0.62	0.64	0.61	0.50
P value Unpaired t Test		0.0160	0.0395	0.0197	0.0098	0.0076	0.0032	0.8143

By conventional criteria the association between the intervention groups and Visual Analog Score is considered to be statistically significant between 30 minutes-8 hours since $p < 0.05$ as per unpaired t test. In simple terms, in patients belonging to Nalbuphine intervention group, the mean Visual Analog Score is decreased to an average of 0.84 points in comparison with patients belonging Tramadol intervention group in whom the mean Visual Analog Score is an average of 1.15 points. The mean Visual Analog Score was meaningfully less in Nalbuphine intervention group compared to Tramadol intervention group by a mean difference of 0.31 points. This significant difference of 27% decrease in mean Visual Analog Score in Nalbuphine intervention group compared to Tramadol intervention group is true and has not occurred by chance.

This indicates that there is a true difference among intervention groups and the difference is significant with a p-value of 0.0160, 0.0395, 0.0197, 0.0098, 0.0076 and 0.0032 according to unpaired t-test. In this study we can safely conclude that Nalbuphine results in significantly decreased mean Visual Analog Score compared to Tramadol when used on postoperative pain and as postoperative analgesic for patients undergoing percutaneous nephrolithotomy.

RESCUE ANALGESIA INITIATION TIME :

The time to initiation of rescue analgesic (inj.diclofenac) in the two groups were as follows,



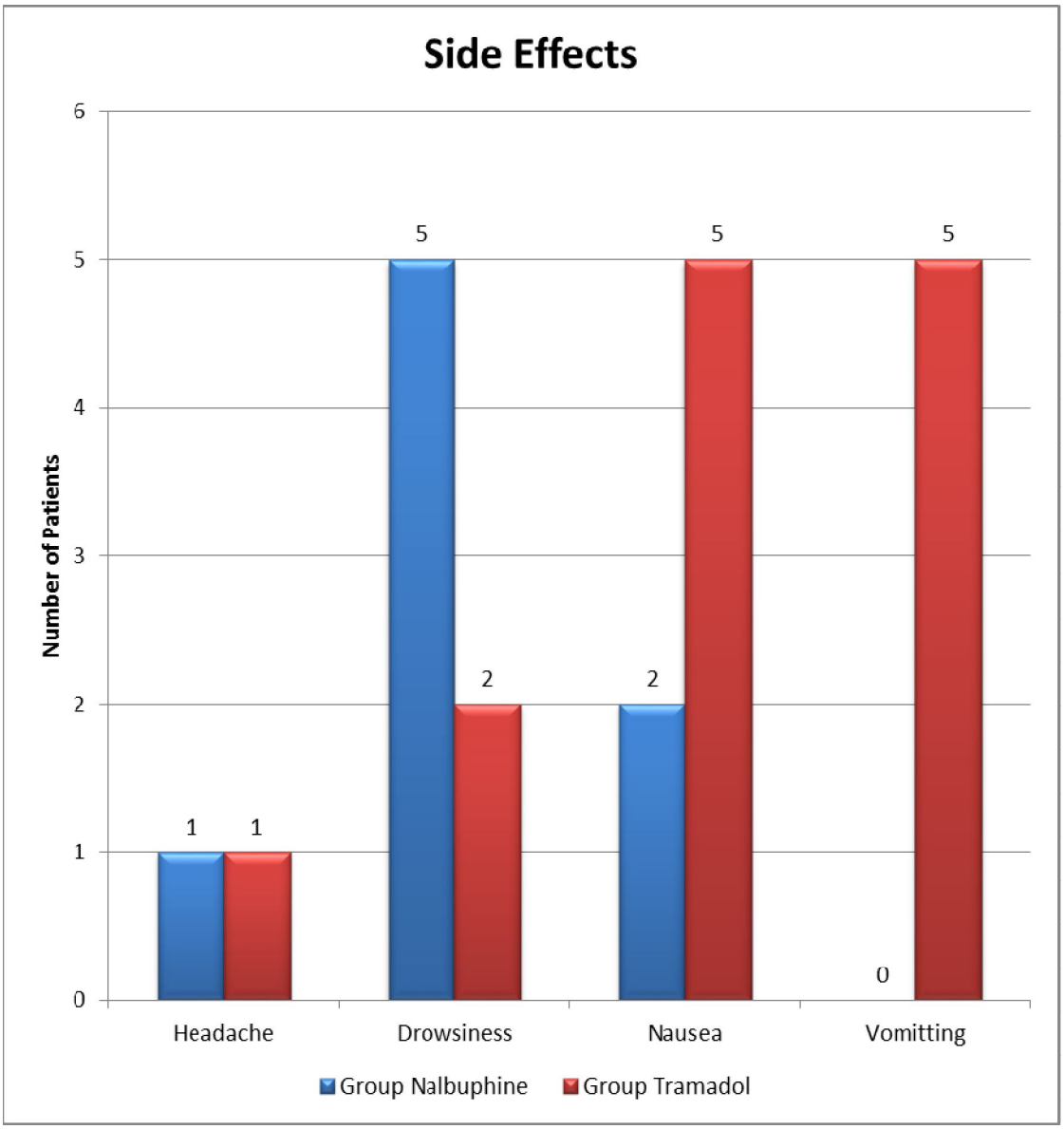
Postoperative Rescue Analgesia Initiation Time	Group Nalbuphine	%	Group Tramadol	%
8 hours	21	70.00	26	86.67
10 hours	9	30.00	4	13.33
Total	30	100	30	100

Postoperative Rescue Analgesia Initiation Time	Group Nalbuphine	Group Tramadol
N	30	30
Mean	8.60	8.27
SD	0.93	0.69
P value Unpaired t Test		0.121609

Majority of the Nalbuphine Group patients belonged to the 8 hours Postoperative Rescue Analgesia Initiation Time class interval (n=21, 70%) with a mean Postoperative Rescue Analgesia Initiation Time of 8.60 hours. In the Tramadol group patients, majority belonged to the 8 hours Postoperative Rescue Analgesia Initiation Time class interval (n=26, 86,67%) with a mean Postoperative Rescue Analgesia Initiation Time of 8.27 hours. The association between the intervention groups and Postoperative Rescue Analgesia Initiation Time is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

SIDE EFFECTS :

The side effects which occurred in the two groups were as follows,



Side Effects	Group Nalbuphine	%	Group Tramadol	%	P value| Fishers Exact Test
Headache	1	3.33	1	3.33	>0.9999
Drowsiness	5	16.67	2	6.67	0.4238
Nausea	2	6.67	5	16.67	0.4238
Vomiting	0	0.00	5	16.67	0.0522

Majority of the Nalbuphine Group patients had drowsiness as the major side effect (n=5, 16.67%). In the Tramadol group patients, majority had nausea and vomitting as the major side effect (n=5, 16.67%). The association between the intervention groups and side effects is considered to be not statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

DISCUSSION :

There are a number of reasons for the undertreatment of postoperative pain. This includes lack of knowledge about the dose ranges, the duration of action of drugs, and also the fear of addiction and respiratory depression.

This prospective, randomized study was done to find a drug, which provided good relief of postoperative pain, in this study, we compared nalbuphine, an opioid agonist – antagonist with tramadol, which is very commonly used for relief of postoperative pain.

The demographic profile of the patients in the study did not show any sifnificant difference.

The nature of postoperative pain varies from one person to another due to factors like age, sex, nature of procedure, psychological makeup of patient.

All the pain evaluations were made by the same observer. Also, the premedication and the anaesthetic techniques used were similar. Equianalgesic doses of drugs were used, which was determined by previews and previous studies.

The patients were divided into two groups,

GROUP A (NALBUPHINE) : they received a bolus dose of 0.2 mg/kg nalbuphine iv , 30 minutes before extubation

GROUP B (TRAMADOL) : they received a bolus dose of 1 mg/kg tramadol iv, 30 minutes before extubation.

At 30 minutes, the percentage of pain relief in nalbuphine group was highly significant as compared to tramadol group. Mean VAS in nalbuphine group was 1.33 and mean VAS in tramadol group was 1.70 at 30 mins.

Visual analog score between 30 minutes-8 hours was statistically significant since $p < 0.05$ as per unpaired t test. In other words, in patients belonging to Nalbuphine intervention group, the mean Visual Analog Score decreased to an average of 0.84 points. In comparison, in patients belonging to the Tramadol intervention group, the mean Visual Analog Score is an average of 1.15 points. The mean Visual Analog Score was meaningfully less in Nalbuphine intervention group when compared to Tramadol intervention group by a mean difference of 0.31 points. This significant difference of 27% decrease in mean Visual Analog Score in Nalbuphine intervention group when compared to Tramadol intervention group has not occurred by chance and hence is true. This indicates that there is a true difference among the two intervention groups and the difference is significant with a p-value of 0.0160, 0.0395, 0.0197, 0.0098, 0.0076 and 0.0032 according to unpaired t-test.($p<0.05$).

The cardiovascular parameters monitored were systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR). The mean changes in these parameters did not show any statistically significant difference between two groups. ($p > 0.05$). Siddiqui et al and Ouaki

et al also showed that there was no hemodynamic significance between the two groups.

The respiratory parameters which were monitored were respiratory rate (RR) and oxygen saturation (SpO2). There was no statistical significance in these parameters between the two groups. ($p > 0.05$). The respiratory parameters were also comparable in the study by Shaila et al and Ouaki et al.

The mean postoperative Rescue Analgesia Initiation Time in nalbuphine group was about 8.60 hours. In the Tramadol group, the mean Postoperative Rescue Analgesia Initiation Time was 8.27 hours. The association between the intervention groups and Postoperative Rescue Analgesia Initiation Time is considered not to be statistically significant since $p > 0.05$ as per 2 tail unpaired t test.

Nalbuphine group showed an increased incidence of drowsiness (16.67%) when compared to the tramadol group (6.67). Shaila et al also had an increased incidence of drowsiness (12.5%) in the nalbuphine group. However, the incidence of nausea and vomiting was more in the tramadol group (16.67%) when compared to nalbuphine group, which had nausea (6.67%) and none of them had vomiting. This is in concordance with studies by Solanki et al and Shaila et al, which had an increased occurrence of nausea and vomiting in tramadol group.

These findings were similar to the results of Shaila et al , which stated that nalbuphine was a safe and effective analgesic for postoperative pain than tramadol.

The safety profile of nalbuphine is been widely accepted by many studies such as those by Siddiqui et al, Ouaki et al, Van Den Berg et al, Shaila et al and Solanki et al.

SUMMARY

"This study was conducted to compare the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy"

The following observations were made:

The mean visual analog score was less in nalbuphine group when compared to tramadol group from 30 minutes to 8 hours time intervals, which was statistically significant. The duration of action of both the drugs was about 8 hours as the time to rescue analgesia was similar in both the groups and statistically insignificant.

In both the groups , the hemodynamic changes and respiratory parameters in the post operative period were comparable and insignificant.

The nalbuphine group showed an increased occurrence of drowsiness, while tramadol group showed an increased occurrence of nausea and vomiting, though there was no statistically significant difference between two groups with respect to side effects.

CONCLUSION

It was concluded that nalbuphine appears to be an effective and safe analgesic for postoperative pain relief than tramadol in equianalgesic doses, in patients undergoing percutaneous nephrolithotomy, providing good sedation with minimum circulatory effects.

REFERENCES

1. Indian J Endocrinol Metab. 2012 Mar-Apr; 16(2): 228–235. Salaman ranabir, Manash.p.baruah, and Reetu devi.
2. Medical Bulletin 14. Dr.Bill, vol.14 no.10 october 2009, 14-17.
3. Michel MS, Trojan L, Rassweiler JJ. Complications in percutaneous nephrolithotomy. Eur Urol. 2007;51:899–906.
4. Pharmacology and physiology in clinical practice, Robert.K.Stoelting, 4th edition, 117-119
5. Raffa RB, Friderichs E, Reimann W. Opioid and nonopioid components independently contribute to the mechanism of action of tramadol, an "atypical" opioid analgesic. J Pharmacol Exp Ther. 1992;260:275–285.
6. Clinical anaesthesia ,Paul.G.Barash, 7th edition, 1612-1617.
7. Miller's anaesthesia, Ronald.D.Miller, 7th edition, 2758-59.
8. Desborough.J.P. , "The stress response to trauma and surgery," British Journal of Anaesthesia, vol. 85, no. 1, pp. 109–117, 2000.
9. Girish P. Joshi .Consequences of inadequate postoperative pain relief and chronic persistant postoperative pain. Anesthesiology Clin N America 2005;23:21-36.
10. Ed Charlton. Practical procedures: The management of post operative pain. Updates in Anesthesia 1997;7:2-17.
11. Indian Journal of Pain, Praveen kumar, Lakshmi tripathi, Year : 2014 ,Volume : 28 ,Issue : 2 , Page : 61-70.
12. Minai FN, Khan FA; A comparison of morphine and nalbuphine for intraoperative and postoperative analgesia. J Pak Med Assoc., 2003; 53(9): 391-396.

13. Khalid Maudood Siddiqui, Ursula Chohan. Tramadol versus Nalbuphine in total intravenous anaesthesia for Dilatation and Evacuation. JPMA 2007; 57:67.
14. Kenan Kaygusuz, Gokhan Gokce, Iclal Ozdemir Kol, Semih Ayan, and Sinan Gursoy**.** Efficacy of Preventive Analgesia with Tramadol or Lornoxicam for Percutaneous Nephrolithotomy: A Prospective, Randomized, Double-Blind, Placebo-Controlled Study Curr Ther Res Clin Exp. 2007 Jul; 68(4): 205–216.
15. Ouaki, J.; Rochette, A.; Raux, O.; Dadure, Ch.; Capdevila, X. Tramadol vs nalbuphine: analgesic efficacy and side effects. A prospective, randomized, double-blinded study in children. European Journal of Anaesthesiology: June 2007- Vol 24- issue- p 138-139.
16. Van den Berg AA, Montoya-Pelaez LF, Halliday EM, Baloch MS; Analgesia for adenotonsillectomy in children and young adults: a comparison of tramadol, pethidine and nalbuphine. European Journal of Anaesthesiology, 1999; 16(3):186-194.
17. Shaila S. Kamath, Arun kumar B .C., Madhusudan Upadya, Sonal Bhat.A comparison of the analgesic effect of intravenous nalbuphine and tramadol in patients with post-operative pain. A double blind prospective randomised study. Asian Journal of Pharmaceutical and Health Services.2013;13:786-90.
18. Shiv Akshat, Rashmi Ramachandran, Vimi Rewari, Chandralekha, Anjan Trikha, and Renu Sinha. Morphine versus Nalbuphine for Open Gynaecological Surgery: A Randomized Controlled Double Blinded Trial. Pain Research and Treatment. Volume 2014 (2014), Article ID 727952, 6 pages.

19. Ananda Bangera, Krishna Prasad P, Prithvi M. Nalbuphine as an Alternate Analgesic toMorphine in Total Abdominal Hysterectomy: A Prospective, Randomized, Comparative, Double-Blind Study. Scholars Journal of Applied Medical Sciences (SJAMS) .. Sch. J. App. Med. Sci., 2015; 3(2E):888-896.
20. Solanki R, N D Gosai, G M Joshi, B M Patel, H V Modi, R Jain. A Comparative Study of Intravenous Nalbuphine HCl and Tramadol HCl for Post- Operative Pain Relief Following Orthopaedic Surgeries. asian pacific journal of health sciences, 2015; 2(1): 155-160.
21. Naguib M, Seraj M, Attia M. Perioperative antinociceptive effects of tramadol. A prospective, randomized, double-blind comparison with morphine. Can J Anaesth. 1998;45:1168–1175.

ANNEXURES

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.M.Suresh
Postgraduate M.D.(Anaesthesia)
Madras Medical College
Chennai 600 003

Dear Dr.M.Suresh,

The Institutional Ethics Committee has considered your request and approved your study titled **"A prospective, randamised study comparing the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy" No.23072015.**

The following members of Ethics Committee were present in the meeting held on 07.07.2015 conducted at Madras Medical College, Chennai-3.

1.	Prof.C.Rajendran, M.D.,	: Chairperson
2.	Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3.	Prof.Sudha Seshayyan, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4.	Prof.B.Vasanthi, M.D., Professor Pharmacology, MMC	: Member
5.	Prof.P.Ragumani, M.S., Professor, Inst.of Surgery, MMC	: Member
6.	Prof.Md.Ali, M.D., D.M., Prof. & HOD of Medl.G.E., MMC	: Member
7.	Prof.Baby Vasumathi, Director, Inst.of O&G, Ch-8	: Member
8.	Prof.K.Ramadevi, Director, Inst.of Biochemistry, MMC	: Member
9.	Prof.Saraswathy, M.D., Director, Inst. Of Pathology, MMC	: Member
10.	Prof.Srinivasagalu, Director, Inst of Inter Med. MMC	: Member
11.	Thiru S.Rameshkumar, B.Com., MBA	: Lay Person
12.	Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
13.	Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE

INFORMATION TO PARTICIPANTS

Investigator: Dr.M.SURESH

Name of the Participant:

Title:

"A Prospective, randomized study comparing the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy "

You are invited to take part in this research study.We have got approval from the IEC. Your are asked to participate because you satisfy the eligibility criteria.We want to compare and study the safety and efficacy of intravenous nalbuphine and intravenous tramadol on post operative pain relief in patients undergoing elective percutaneous nephrolithotomy.

What is the Purpose of the Research:

To compare the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy, based on

Post-operative VAS score

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR) and oxygen satuiration(Spo2) were measured at baseline and at intervals of 1,5,10,15,30min and 1,2,3,4,5,6,8,10,12 and 24hours
Post operative rescue analgesia requirement

The Study Design:

60 Patients presenting for elective percutabneous nephrolithotomy were randomly assigned into two groups.

GROUP A(Nalbuphine) : received a bolus dose of 0.2mg/kg IV 30 mins before extubation

GROUP B (Tramadol) : received a bolus dose of 1mg/kg IV 30 mins before extubation

.**Benefits**

The usage of nalbuphine and tramadol when administered intraoperatively, maintains better post operative hemodynamics , causing excellent post operative pain relief.

Discomforts and risks

May cause nausea, vomiting, drowsiness, headache, anaphylactic reactions.

This intervention has been shown to be well tolerated as shown by previous studies.And if you do not want to participate you will have alternative of setting the standard treatment and your safety is our prime concern.

All tests, medicine and medical services concerned with this research will be provided free of cost to the patient.

Time and date :
Place :

Signature of the Investigator : _____ Signature / Thumb Impression of patient

Name of the Investigator : _____ Patient name :

PATIENT CONSENT FORM

Study Title :

"A Prospective, randomized study comparing the analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy"

Study center:
Institute of Anaesthesiology and Critical Care,
Madras Medicalcollege,
Chennai- 600003.

Participant name : Age: Sex: I.P.No:

I confirm that I have understood the purpose of the above study . I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the safety,advantage and disadvantage of the drugs.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator ,regulatory authorities and the ethical committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study . I understand that my identity will not be revealed in any information released to third parties or published , unless as required under the law . I agree not to restrict the use of any data or results that arise from the study .

Time:

Date: Signature/thumb impression of patient

Place: Patient name:

Signature of the investigator: Name of the investigator:

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சியாளர் பெயர் : மருத்துவர்.ம.சுரேஷ்

பங்கேற்பாளர் பெயர் :

ஆராய்ச்சி தலைப்பு

தோல்வழி சிறுநீரக கல் நீக்க அறுவை சிகிச்சையில் அறுவை சிகிசிச்சைக்குப் பின் இரத்த நாள (சிரை) வழி நால்புபின் அல்லது டிரமடால் வழங்குவதன் மூலம் கிடைக்கும் வலி நிவாரணம் மற்றும் வலி நிவாரண மருந்துகளின் தேவையை ஒப்பிடும் முன்னோக்கு ஆய்வு

ஆராய்ச்சியின் நோக்கம்

தோல்வழி சிறுநீரக கல் நீக்க அறுவை சிகிச்சைக்கு வரும் நோயாளிகளுக்கு சிகிச்சையின்போது நால்புபின் அல்லது டிரமடால் இரத்த நாள (சிரை) வழியாக கொடுக்கப்படும். இவ்வாய்வு கீழ்கண்ட கோணங்களில் ஒப்பிடப்படுகிறது.

1) நாடித்துடிப்பு இரத்த அழுத்தம் மற்றும் சுவாச அளவு ஆகியவை 1, 5, 10, 15, 30 நிமிடங்களில் மற்றும் 1, 2, 3, 4, 5, 6, 8, 10, 12, 24 மணி நேரங்களில் கணக்கிடப்படும்.
2) அறுவை சிகிச்சைக்குப்பின்னர் ஏற்படும் வலி நிவாரணம் கணக்கிடப்படுகிறது.
3) அறுவை சிகிச்சைக்குப்பின்னர் தேவைப்படும் வேறு வலி நிவாரண மருந்துகளின் தேவையும் கணக்கிடப்படுகிறது.

ஆய்வு முறை

ஆய்வில் பங்குபெறும் நோயாளிகள் இரண்டு குழுக்களாகப் பிரிக்கப்படுவர்.

குழு-அ நால்புபின் 0.2 மி.கி/கிலோ, செயற்கை சுவாசக்குழாய் எடுப்பதற்கு 30 நிமிடங்களுக்கு முன் இரத்தநாள (சிரை) வழியாக கொடுக்கப்படும்.

குழு-ஆ டிரமடால் 1 மி.கி/கிலோ, செயற்கை சுவாசக்குழாய் எடுப்பதற்கு 30 நிமிடங்களுக்கு முன் இரத்தநாள (சிரை) வழியாக கொடுக்கப்படும்.

நன்மைகள்

1) அறுவை சிகிச்சைக்குப்பின்னர் ஏற்படும் நாடித்துடிப்பு மற்றும் இரத்த அழுத்த மாற்றங்கள் குறைக்கப்படுகிறது.
2) அறுவை சிகிச்சைக்குப் பின்னர் வலி நிவாரணத்தின் தன்மை நீட்டிக்கப்படுகின்றது.
3) இதர வலி நிவாரண மருந்துகளின் தேவைகள் வெகுவாக குறைக்கப்படுகிறது.

பக்கவிளைவுகள்

குமட்டல், வாந்தி, தலைவலி, அசதி ஏற்படலாம். அதற்கு மாற்று மருந்துகள் உடனடியாக கொடுக்கப்படும்.

இந்த ஆய்வு சம்பந்தமான எல்லா புள்ளி விவரங்கள் மற்றும் நோயாளிகளின் விவரங்கள் ரகசியமாக வைக்கப்படும். இந்த ஆய்வு சம்பந்தப்பட்ட எல்லா பரிசோதனைகள், மருந்துகள் மற்றும் மருத்துவ சேவைகள் அனைத்தும் நோயாளிகளுக்கு இலவசமாக வழங்கப்படும்.

நீங்கள் இந்த ஆய்வில பங்குகொள்ள விரும்பவில்லை என்றால் எப்போதும் உபயோகப்படுத்தும் முறையில் மருந்து கொடுக்கப்படும். உங்கள் பாதுகாப்பே எங்களின் முக்கிய நோக்கம்.

சாட்சியின் கையொப்பம்

பெயர்:

பங்குபெறுபவரின் கையொப்பம்
இடது கட்டைவிரல் ரேகை

பெயர்:

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராயச்சியின் தலைப்பு

தோல்வழி சிறுநீரக கல் நீக்க அறுவை சிகிச்சையில் அறுவை சிகிசிச்சைக்குப் பின் இரத்த நாள (சிறை) வழி நால்புபின் அல்லது டிரமடால் வழங்குவதன் மூலம் கிடைக்கும் வலி நிவாரணம் மற்றும் வலி நிவாரண மருந்துகளின் தேவையை ஒப்பிடும் முன்னோக்கு ஆய்வு

ஆய்வு நிலையம் : மயக்கவியல் துறை, சென்னை மருத்துவக் கல்லூரி சென்னை - 3.

பங்கு பெறுவரின் பெயர் :

பங்குபெறுபவரின் எண் :

பாலினம் :

பங்குபெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் 'இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிகிறேன். ☐

அறுவை சிகிச்சையின்போது இரத்த நாள (சிறை) வழியாக நால்புபின் அல்லது டிரமடால் வழங்கப்படும் என்பதை அறிந்துகொண்டேன். இதனால் உடலுக்கு எந்தவிதமான உபாதைகளும் இருக்காது என்பதை அறிந்துகொண்டு இந்த ஆய்வில் பங்குபெற முழு மனதுடன் சம்மதிக்கிறேன். ☐

நேரம் :

நாள் :

இடம் :

கலந்துகொள்பவரின் கைரேகை/
கையொப்பம்
பெயர்

ஆய்வாளரின் கையொப்பம் :

ஆய்வாளரின் பெயர் :

PROFORMA

Date: Roll no:

Name:

Age: Ht:Wt: Sex: IP No:

Diagnosis:

Surgical procedure:

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

H/O Documented Difficult Airway

H/O previous surgeries

EXAMINATION : CVS : RS : Hb :

MEASURES OF STUDY OUTCOME:

	HR	SBP	DBP	MAP	RR	Spo2	VAS SCORE
PRE OP							
INTRA OP(AT THE TIME OF DRUG ADMINISTRATION)							
1 MIN							
5 MIN							
10 MIN							
15 MIN							
30 MIN							
1 HR							
2 HR							
4 HR							
5 HR							
6 HR							
8 HR							
10 HR							
12 HR							
24 HR							

COMPLICATIONS/ SIDE EFFECTS IN POST OPERATIVE PERIOD:

RESCUE ANALGESICS USED:

GROUP 1 (NALBUPHINE GROUP)																								
							BASELINE VITALS							POSTOPERATIVE HR (BEATS / MIN)										
SERIAL NO	NAME	AGE/ SEX	WEIGHT (KGS)	HEIGHT (METERS)	BMI (KG/M2)		SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	HR /min	RR / min	SpO2 %		10 MINS	15	30	60	2 HRS	3	4	6	8	10	
1	SUMATHI	38/F	57	1.54	24.03		116	70	85	76	13	99		86	83	77	75	74	77	76	78	82		
2	LOGESWARI	37/F	59	1.52	25.53		127	83	98	92	12	99		108	106	94	95	89	82	84	86	92		
3	TAMILARASI	45/F	53	1.51	23.24		116	75	89	77	12	99		88	85	84	79	78	80	84	89	86	89	
4	ASIRVATHAM	43/M	65	1.65	23.87		118	73	88	73	14	99		93	89	90	86	86	84	80	92	89		
5	PARAMASIVAM	45/M	67	1.7	23.18		127	87	100	87	15	98		103	96	98	94	87	90	86	81	83		
6	SUNDHARAM	48/M	62	1.65	23.77		121	83	96	84	13	99		84	81	85	76	73	70	74	75	81	84	
7	SUBRAMANI	57/M	65	1.64	24.16		130	84	99	87	12	98		99	101	96	89	92	90	86	84	82		
8	ARAVIND	38/M	71	1.72	23.99		126	79	95	92	11	99		110	108	104	99	86	88	90	87	86		
9	SELVARAJ	57/M	60	1.66	21.77		123	81	95	88	16	98		94	94	92	87	83	76	81	82	92		
10	RAJKUMAR	28/M	69	1.7	23.87		112	77	89	69	14	99		87	85	80	77	70	73	77	70	72	83	
11	VITLA	40/F	57	1.52	24.67		121	73	89	74	13	99		95	97	90	81	69	72	76	74	77		
12	MADURAPANDI	47/M	63	1.65	23.14		117	73	88	77	12	99		83	84	79	73	77	81	83	79	85		
13	RAJESHWARI	49/F	58	1.55	24.14		109	68	82	62	13	98		80	82	74	68	70	67	68	64	67		
14	SATHYANARAYANAN	41/M	61	1.63	22.95		113	71	85	78	14	99		98	103	90	85	83	83	85	77	80	89	
15	JEEVA	27/M	69	1.68	24.44		116	74	88	80	13	99		106	105	92	87	80	77	84	81	79		
16	SHANMUGAM	60/M	67	1.62	25.52		124	86	99	67	12	98		88	93	89	79	74	77	75	69	70		
17	SURESH BABU	45/M	74	1.67	26.53		113	71	85	73	12	99		97	94	96	87	79	83	79	74	70		
18	MURUGAN	49/M	68	1.64	25.28		108	65	79	67	12	99		80	87	89	83	78	80	83	69	68	82	
19	SUMATHI	20/F	49	1.54	20.66		110	67	81	70	14	99		92	97	95	90	87	81	79	75	75		
20	MARIYAMMAL	55/F	52	1.53	22.21		117	71	86	74	13	98		91	93	87	83	88	79	81	72	74	85	
21	VELU	45/M	63	1.6	24.6		127	77	94	81	12	99		105	102	91	86	83	77	80	83	87		
22	JEYA	55/F	53	1.49	23.87		123	78	93	77	12	98		97	99	89	80	74	72	74	79	88		
23	ANIL KUMAR	40/M	63	1.61	24.3		116	70	85	72	15	99		97	93	90	79	76	78	69	74	77		
24	KARIKALAN	37/M	65	1.67	23.3		127	75	92	80	14	99		106	102	91	77	76	67	68	80	82		
25	SYED ALI FATHIMA	42/F	50	1.56	20.54		123	69	87	71	12	99		110	106	98	90	85	81	79	85	83	95	
26	VISALATCHI	57/F	54	1.52	23.37		109	63	78	67	12	98		87	88	79	85	78	71	72	76	79	87	
27	NARASIMMAN	32/M	69	1.63	25.97		134	92	106	94	13	99		99	100	98	92	83	74	77	82	86		
28	THIRUMOORTHY	28/M	67	1.69	23.45		120	82	95	81	12	99		106	102	101	94	87	70	79	80	77		
29	IRSHAD AHMED	45/M	64	1.62	24.38		130	85	100	77	15	99		85	87	92	86	90	77	82	77	81	92	
30	VASANTHA	50/F	55	1.53	23.49		113	70	84	68	13	98		79	79	81	84	88	79	80	76	79		

POSTOPERATIVE SBP (mmHg)											POSTOPERATIVE DBP (mmHg)									
10 MINS	15	30	60	2HRS	3	4	6	8	10		10 MINS	15	30	60	2 HRS	3	4	6	8	10
126	121	119	117	109	112	114	117	123			85	83	79	76	70	68	73	70	73	
132	127	121	124	115	117	119	123	125			87	86	80	79	73	71	70	81	73	
125	128	120	118	114	110	106	112	115	126		79	83	77	74	74	72	68	73	69	
130	133	137	130	123	117	109	111	109			81	81	83	79	81	77	68	74	65	79
133	131	126	124	120	125	119	113	120			85	80	71	72	77	76	72	77	82	
126	125	122	121	117	121	117	115	124	129		84	84	75	74	75	78	71	70	81	
140	137	134	129	121	117	114	117	118			92	90	83	81	79	81	77	78	76	82
129	129	132	126	117	113	117	116	115			81	86	84	82	84	82	83	85	75	
129	131	125	117	110	111	123	119	123			87	83	81	70	73	77	69	70	86	
119	117	116	110	106	106	109	113	116	121		77	80	74	69	67	73	70	69	75	
127	129	132	127	123	117	121	122	121			79	81	76	79	70	68	74	73	70	77
123	122	114	109	110	112	117	125	120			81	77	69	66	65	68	77	76	81	
115	114	124	115	113	111	115	124	123			74	69	73	69	71	69	70	72	71	
119	123	130	122	117	115	111	112	117	130		80	68	79	73	74	73	72	72	77	
126	129	126	119	112	117	119	117	115			82	80	72	75	69	73	68	67	75	83
123	119	124	125	118	121	124	121	126			84	73	84	80	67	77	74	81	82	
117	121	113	117	113	117	120	117	123			80	72	79	75	70	68	73	80	80	
120	127	125	114	110	113	110	115	114	129		82	77	76	69	73	75	79	85	84	
115	110	119	120	106	109	106	112	117			77	68	71	77	78	79	81	82	87	86
119	123	127	123	112	109	107	115	115	131		78	87	82	73	71	77	80	77	80	
131	134	132	127	115	117	113	113	114			87	84	81	75	76	81	73	71	82	85
130	126	119	112	107	105	109	112	120			88	79	74	68	70	70	71	70	69	
126	123	120	119	113	112	117	121	127			85	75	70	73	74	72	72	68	68	
137	140	145	129	115	111	114	120	132			96	80	82	79	80	78	81	72	79	
130	132	130	120	123	119	109	118	130	139		92	81	81	80	82	83	80	73	81	
121	125	128	123	119	121	122	118	124	130		84	82	74	72	70	80	84	81	87	85
145	139	137	129	123	117	117	114	113			100	91	84	74	68	73	79	85	82	83
132	130	131	119	110	118	113	115	119			87	79	80	75	73	74	80	82	84	
141	136	127	118	107	109	110	116	119	120		108	94	82	79	80	75	81	79	88	79
130	132	124	119	113	107	106	112	125			79	81	73	70	68	70	75	77	81	

POSTOPERATIVE MAP (mmHg)											RESPIRATORY RATE (/MIN)									SpO2 (%)			
10 MINS	15	30	60	2 HRS	3	4	6	8	10		30 MINS	60	2 HRS	3	4	6	8	10		30MINS	60	2HRS	3
99	96	92	90	83	83	87	86	90			16	12	11	13	12	13	12			98	99	99	99
102	100	94	94	87	86	86	95	90			12	12	13	14	13	12	11			99	98	99	99
94	98	91	89	87	85	81	86	84	95		13	12	12	12	15	12	13	15		99	98	99	99
97	98	101	96	97	90	82	86	80			14	13	14	12	11	15	14			98	99	98	99
101	97	89	89	91	92	88	89	95			12	13	12	11	13	14	15			99	99	99	99
98	98	91	90	89	92	86	85	95	98		15	13	12	13	14	13	12	14		98	99	99	99
108	106	100	97	93	93	89	91	90			14	12	11	12	12	13	10			99	98	99	99
97	100	100	97	95	92	94	95	88			13	12	11	12	12	12	13			99	99	99	99
101	99	96	86	85	88	87	86	98			14	12	12	13	13	12	14			98	98	99	99
91	92	88	83	80	84	83	84	89	92		15	13	11	11	14	13	12	15		98	99	98	98
95	97	95	95	88	84	90	89	87			12	11	12	13	15	13	11			98	99	99	99
95	92	84	80	80	83	90	92	94			13	12	13	12	13	13	15			98	98	99	99
88	84	90	84	85	83	85	89	88			11	13	12	12	12	12	15			99	98	98	99
93	86	96	89	88	87	85	85	90	99		13	12	12	13	14	14	12	16		98	99	99	99
97	96	90	90	83	88	85	84	88			17	12	12	15	14	13	13			99	99	99	99
97	88	97	95	84	92	91	94	97			12	13	11	12	12	12	14			99	99	99	99
92	88	90	89	84	84	89	92	94			14	13	12	11	12	14	11			98	99	99	99
95	94	92	84	85	88	89	95	94	100		13	12	12	10	11	12	10	14		97	98	98	98
90	82	87	91	87	89	89	92	97			16	14	13	13	13	12	12			98	99	99	99
92	99	97	90	85	88	89	90	92	100		12	12	12	12	12	13	12	14		99	99	99	99
102	101	98	92	89	93	86	85	93			13	13	12	14	11	13	15			99	98	99	99
102	95	89	83	82	82	84	84	86			14	12	11	12	14	14	16			98	99	99	99
99	91	87	88	87	85	87	86	88			12	12	12	13	12	13	13			99	99	99	99
110	100	103	96	92	89	92	88	97			13	14	11	13	13	12	11			99	99	99	99
105	98	97	93	96	95	90	88	97	103		13	12	13	12	12	14	10	15		98	98	99	99
96	96	92	89	86	94	97	93	99	99		13	13	12	12	13	12	12	15		98	99	99	99
115	107	102	92	86	88	92	95	92			12	12	11	12	13	13	13			98	98	99	99
102	96	97	90	85	89	91	93	96			12	11	12	13	12	12	12			99	99	99	99
119	108	97	92	89	86	91	91	98	93		14	13	12	12	12	13	12	14		98	99	99	98
96	98	90	86	83	82	85	89	96			12	12	12	13	13	12	13			99	99	99	99

		SpO2				VISUAL ANALOOG SCORE (HRS)							POSTOPERATIVE RESCUE ANALGESIA INITIATION TIME (HRS)		COMPLICATIONS/ SIDE EFFECTS			
4	6	8	10		30 MINS	1	2	4	6	8	10		INJ DICLOFENAC INTRAMUSCULAR		HEADACHE	DROWSINESS	NAUSEA	VOMITING
99	99	99			1	0	0	0	0	3			8					
99	99	99			1	0	0	0	1	3			8					
99	99	99	99		1	0	0	0	1	1	3		10				yes	
98	99	98			2	1	1	0	0	3			8			yes		
99	99	99			1	0	0	0	1	3			8					
99	98	98	98		2	1	0	0	0	1	3		10					
99	99	99			1	1	1	0	1	3			8					
98	99	99			2	0	0	0	0	3			8			yes		
99	99	99			2	1	1	0	1	3			8					
99	99	99	99		1	0	0	0	0	2	4		10		yes			
99	99	98			2	1	1	1	1	3			8					
99	98	99			1	0	0	0	0	3			8					
99	99	98			2	0	0	0	1	3			8					
98	99	99	99		1	0	0	0	0	1	3		10					
99	99	99			1	1	0	0	1	3			8					
99	99	99			0	0	0	0	1	3			8			yes		
99	99	99			1	0	0	0	0	3			8					
99	99	99	99		1	0	0	0	1	1	3		10			yes		
99	99	99			1	0	0	0	1	3			8					
99	98	99	98		2	1	0	0	0	2	4		10					
99	99	99			1	0	0	0	1	3			8					
99	99	99			1	0	0	0	0	3			8			yes		
99	99	98			2	0	0	0	1	3			8					
99	99	99			2	1	1	1	2	3			8					
99	99	99	99		1	0	0	0	0	2	4		10					
99	99	99	99		2	0	0	0	0	2	4		10					
99	99	99			1	1	0	0	1	3			8				yes	
99	99	99			1	0	0	0	0	3			8					
99	99	99	99		2	1	1	0	1	2	5		10					
99	99	99			1	0	0	0	0	3			8					

GROUP 2 (TRAMADOL GROUP)																						
							BASELINE VITALS							POSTOPERATIVE HR (BEATS/MIN)									
SERIAL NO	NAME	AGE/ SEX	WEIGHT (KGS)	HEIGHT (METERS)	BMI (KG/M2)		SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	HR /min	RR / min	SpO2 %		10 MINS	15	30	60	2 HRS	3	4	6	8	10
1	SARASWATHY	45/F	52	1.54	21.92		123	82	96	81	13	99		98	99	93	88	86	84	80	76	77	
2	RAMAN	52/M	64	1.67	22.94		129	87	101	71	14	98		110	108	102	92	88	83	76	69	70	
3	SARADHA	45/F	49	1.51	21.49		121	77	92	78	15	98		88	90	86	84	85	81	79	70	68	79
4	SUSEELA	35/F	51	1.56	20.95		117	76	90	67	13	99		93	97	89	86	86	87	77	78	74	
5	ANTHONYSAMY	40/M	69	1.7	23.87		115	73	87	91	12	99		92	88	82	83	81	77	83	79	83	
6	CHANDRASEKA	34/M	63	1.68	22.32		124	83	97	84	13	99		93	90	84	81	80	76	78	81	84	
7	GOKULRAJ	26/M	60	1.65	22.03		118	79	92	77	12	99		95	92	85	82	77	73	75	80	83	
8	MAHALAKSHMI	57/F	50	1.46	23.45		109	66	80	65	14	98		87	89	80	80	79	76	77	83	86	
9	JANAKI	44/F	57	1.65	20.93		115	70	85	75	13	99		89	93	81	82	81	78	77	71	79	
10	EKAMBARAM	52/M	70	1.73	23.38		130	82	98	88	15	98		92	90	85	79	76	76	70	67	76	
11	HARISH	23/M	58	1.57	23.53		116	71	86	78	16	99		90	91	87	83	79	75	73	70	68	80
12	SATHIYAVANI	54/F	56	1.48	25.56		112	69	83	87	12	98		87	89	84	79	80	81	85	88	81	
13	SHENBAGAM	48/F	60	1.57	24.34		123	75	91	70	13	99		84	87	86	81	81	83	83	87	85	
14	MUNUSAMY	38/M	65	1.67	23.3		125	79	94	83	12	99		98	92	88	84	80	82	80	86	90	
15	KHALEEL RAHM	59/M	72	1.72	24.33		132	87	102	66	12	98		107	103	101	94	89	90	88	83	81	
16	PARVATHY	40/F	65	1.6	25.39		128	85	99	70	15	99		103	104	98	90	90	88	93	90	97	
17	VIJAYAKUMAR	48/M	68	1.73	22.72		127	76	93	79	13	99		100	99	94	88	85	88	90	88	83	
18	SANGEETHA	21/F	50	1.52	21.64		116	70	85	69	14	99		98	101	95	88	85	87	88	83	78	
19	PAVITHRA	28/F	53	1.58	21.23		111	66	81	72	16	99		96	98	90	83	84	80	79	75	70	85
20	ELUMALAI	43/M	68	1.65	24.97		119	72	88	90	13	99		88	87	80	74	76	78	82	79	86	
21	SUBRAMANI	49/M	69	1.74	22.79		118	74	89	84	14	98		85	89	83	77	78	76	70	71	76	
22	HEMALATHA	50/F	57	1.55	23.72		124	78	93	77	12	98		96	100	93	87	85	83	77	70	74	
23	RAVI	53/M	65	1.65	23.87		126	80	95	76	13	99		101	102	94	88	84	84	75	68	70	83
24	DIVYA	30/F	62	1.67	22.23		114	71	85	81	14	99		98	99	91	90	88	86	88	87	84	
25	SATHIK BASHA	40/M	75	1.65	27.54		128	83	98	66	12	99		105	104	100	92	84	81	85	79	77	
26	RADHIKA	43/F	54	1.59	21.35		115	68	84	78	14	99		86	84	79	73	70	72	76	81	81	
27	GANDHIMATHY	47/F	58	1.55	24.14		108	65	79	82	13	99		79	83	76	71	69	70	79	85	88	
28	MAHENDRAN	33/M	64	1.63	24.08		123	77	92	83	15	99		95	95	86	84	82	77	71	76	79	
29	SELVI	35/F	57	1.58	22.83		114	69	84	70	12	99		102	103	95	89	87	83	78	87	87	
30	CHARAN	29/M	62	1.66	22.49		122	80	94	74	13	99		95	96	88	88	89	86	85	83	88	

POSTOPERATIVE SBP (mmHg)											POSTOPERATIVE DBP (mmHg)									
10 MINS	15	30	60	2 HRS	3	4	6	8	10		10 MINS	15	30	60	2 HRS	3	4	6	8	10
128	131	126	118	111	113	121	119	124			90	84	81	75	78	74	80	81	85	
131	130	126	118	112	109	108	114	126			86	81	74	76	77	73	79	75	84	
130	139	135	128	119	115	112	117	121	129		79	82	74	73	69	73	70	74	83	91
119	124	129	126	117	110	107	113	119			79	82	85	80	72	68	67	71	76	
128	130	127	121	123	118	117	116	120			85	86	81	73	68	77	81	85	82	
123	119	126	125	119	121	127	126	128			81	79	80	68	71	73	84	88	85	
130	132	137	129	124	118	116	113	116			90	84	85	81	80	82	84	84	79	
121	126	127	125	120	117	111	121	124			87	84	79	77	71	76	77	83	81	
126	123	123	118	113	111	118	121	128			85	79	78	70	68	69	73	78	82	
140	136	134	129	125	120	118	121	127			100	94	83	80	82	84	80	83	79	
125	129	118	112	110	106	111	117	121	129		85	81	72	67	70	70	69	72	75	87
121	119	115	110	107	105	110	114	119			87	83	69	65	68	69	70	71	73	
130	133	128	118	110	114	119	123	126			88	85	81	71	75	72	76	79	86	
127	129	132	123	116	112	116	118	117			84	86	85	80	81	75	78	74	85	
141	139	137	130	122	116	116	126	119			94	92	88	84	79	77	80	86	82	
136	140	141	128	123	112	109	117	123			85	91	85	79	78	73	74	75	84	
131	134	127	126	117	113	110	111	114			80	85	80	76	67	71	66	70	80	
127	122	120	117	108	116	112	106	118			79	84	76	70	68	69	78	72	76	
115	110	119	121	108	110	117	111	118	128		75	69	73	77	68	66	77	77	75	86
126	124	121	112	106	111	121	115	126			75	75	74	77	76	78	85	83	85	
130	128	122	119	110	111	118	125	125			82	77	77	79	81	80	84	81	84	
129	132	129	120	123	119	109	117	123			83	84	82	78	79	83	78	79	81	
133	130	127	123	117	121	109	113	119	128		91	86	80	76	81	83	85	84	77	89
120	124	130	124	120	117	113	111	124			84	81	75	72	78	82	78	78	84	
132	126	123	121	119	117	118	123	128			83	84	79	75	83	79	82	84	88	
118	122	116	118	112	105	115	118	120			80	83	75	70	73	70	73	79	79	
121	128	119	112	109	113	109	114	122			84	81	75	66	69	78	75	81	81	
127	129	132	123	117	121	112	118	129			86	86	80	81	77	82	85	80	86	
119	121	117	106	110	105	116	121	119			79	82	72	69	69	76	78	85	80	
131	125	118	115	106	109	113	124	130			85	83	75	76	80	79	80	81	90	

POSTOPERATIVE MAP (mmHg)											RESPIRATORY RATE (/MIN)										SpO2 (%)			
10MINS	15	30	60	2 HRS	3	4	6	8	10		30 MINS	60	2 HRS	3	4	6	8	10			30MINS	60	2HRS	3
103	100	96	89	89	87	94	94	98			18	15	14	13	12	14	13				99	98	99	99
101	97	91	90	89	85	89	88	98			14	13	13	14	15	13	12				98	99	99	99
96	101	94	91	86	87	84	88	96	104		15	13	12	13	14	13	12	15			98	99	99	99
92	96	100	95	87	82	80	85	90			16	14	12	12	12	14	13				99	99	98	99
99	101	96	89	86	91	93	95	95			13	13	12	11	12	12	14				99	98	99	99
95	92	95	87	87	89	98	101	99			18	15	13	13	14	16	13				99	99	99	99
103	100	102	97	95	94	95	94	91			16	14	14	13	12	14	12				98	99	99	99
98	98	95	93	87	90	88	96	95			13	12	12	13	13	12	14				98	98	98	99
99	94	93	86	83	83	88	92	97			15	13	12	12	12	13	12				99	99	99	99
113	108	100	96	96	96	93	96	95			16	14	13	12	13	11	13				98	99	98	98
98	97	87	82	83	82	83	87	90	101		14	15	14	14	13	12	12	16			99	99	99	99
98	95	84	80	81	81	83	85	88			12	13	13	13	14	13	13				98	98	99	99
102	101	97	87	87	86	90	94	100			13	13	12	12	12	12	14				99	99	98	99
98	100	101	94	93	87	91	89	96			12	12	13	14	13	15	15				98	99	99	99
110	108	104	99	93	90	92	99	94			15	14	12	12	12	13	14				97	98	99	99
102	107	104	95	93	86	86	89	97			15	13	12	13	11	13	13				99	99	99	99
97	101	96	93	84	85	81	84	91			13	13	15	13	12	13	10				98	99	99	99
95	97	91	86	81	85	89	83	90			12	13	12	13	12	12	11				98	98	98	98
88	83	88	92	81	81	90	88	89	100		17	14	14	12	13	14	15	15			97	98	98	98
92	91	90	89	86	89	97	94	99			15	13	12	13	12	12	12				99	99	99	99
98	94	92	92	91	90	95	96	98			13	13	13	12	13	13	12				98	99	99	99
98	100	98	92	94	95	88	92	95			15	13	12	12	14	13	13				99	98	99	99
105	101	96	92	93	96	93	94	91	102		13	14	12	14	13	14	14	15			99	98	99	99
96	95	93	89	92	94	90	89	97			12	14	12	13	13	14	13				98	99	99	99
99	98	94	90	95	92	94	97	101			16	15	13	12	13	14	12				99	99	99	99
93	96	89	86	86	82	87	92	93			14	12	14	13	14	13	12				98	99	99	99
96	97	90	81	82	90	86	92	95			14	12	11	12	12	14	13				99	98	99	99
100	100	97	95	90	95	94	93	100			13	11	12	14	13	12	14				98	99	99	99
92	95	87	81	83	86	91	97	93			15	13	12	11	10	12	13				99	98	99	98
100	97	89	89	89	89	91	95	103			13	12	13	13	12	13	11				98	98	98	98

		SpO2				VISUAL ANALOG SCORE (HRS)						POSTOPERATIVE RESCUE ANALGESIA INITIATION TIME (HRS)		COMPLICATIONS/ SIDE EFFECTS			
4	6	8	10	30 MINS	1	2	4	6	8	10		INJ DICLOFENAC INTRAMUSCULAR		HEADACHE	DROWSINESS	NAUSEA	VOMITTING
99	99	99		1	0	0	0	1	3			8				YES	
99	99	98		2	1	1	1	2	4			8					
99	99	99	99	2	0	0	0	1	2	4		10			YES		
99	99	99		2	1	0	0	1	3			8					
99	99	99		1	0	0	0	2	4			8					
99	99	99		3	1	1	1	1	3			8					
99	99	99		1	0	0	0	1	3			8				YES	YES
99	99	99		2	0	0	0	2	4			8					
99	99	99		2	1	1	1	1	3			8					
98	98	98		2	0	0	0	0	3			8					
99	99	99	99	2	0	0	0	1	2	4		10				YES	
99	99	99		2	0	0	0	1	3			8					
99	99	99		2	1	1	2	2	3			8					
99	99	98		1	0	0	0	0	4			8		YES			
99	99	99		2	1	0	0	1	3			8					YES
99	99	99		2	1	1	1	1	3			8					
99	99	99		1	0	0	0	0	3			8				YES	
98	98	98		2	1	0	0	1	3			8					
98	99	99	99	1	0	0	1	1	2	3		10					
99	99	99		3	1	1	2	2	3			8					YES
99	99	99		1	0	0	0	1	4			8			YES		
99	99	99		2	1	1	1	0	3			8					
99	99	99	99	1	0	0	0	1	2	4		10					
99	99	99		2	0	0	0	0	3			8					YES
99	98	98		2	0	0	1	2	4			8					
99	99	99		1	0	0	0	1	3			8					
99	99	99		2	1	1	1	1	3			8				YES	YES
99	99	99		1	0	0	0	1	3			8					
99	99	99		2	1	1	0	0	4			8					
98	98	98		1	0	0	0	1	3			8					